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Trial record **1 of 1** for: TVP-1012/500

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A Randomized Placebo Controlled Study to Show That Rasagiline May Slow Disease Progression for Parkinson's Disease (ADAGIO)

This study has been completed.

Sponsor:
Teva Pharmaceutical Industries

Information provided by (Responsible Party):
Teva Pharmaceutical Industries

ClinicalTrials.gov Identifier:
NCT00256204

First received: November 16, 2005
Last updated: January 10, 2012
Last verified: January 2012
History of Changes

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Purpose

A 2 phase study to evaluate disease progression in Parkinson's disease patients taking rasagiline

Condition	Intervention	Phase
Parkinson's Disease	Drug: Rasagiline Mesylate Other: Placebo	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator)
Primary Purpose: Treatment

Official Title: A Multi Center, Double Blind, Randomized Start, Placebo-Controlled, Parallel-Group Study to Assess Rasagiline as a Disease Modifying Therapy in Early Parkinson's Disease Subjects

Resource links provided by NLM:

Genetics Home Reference related topics: Parkinson disease Perry syndrome

MedlinePlus related topics: Parkinson's Disease

Drug Information available for: Rasagiline mesylate

U.S. FDA Resources

Further study details as provided by Teva Pharmaceutical Industries:

Primary Outcome Measures:

- Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline [Time Frame: 12w, 24w, 36w, 42w, 48w, 54w, 60w, 66w, 72w] [Designated as safety issue: No]

  The primary efficacy endpoint was defined as the change in Total UPDRS from Baseline. Subjects were assessed according to the United Parkinson's Disease Rating Scale (UPDRS,(version 3;) Parts I and II are historical data and are designed to rate mentation, behavior and mood; Part III is done as a motor examination at the time of a visit. The UPDRS measures patient status on a scale 0, which is normal or none, to 4, which is severe or the worst scenario.

Secondary Outcome Measures:

- Change in Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline to Last Observed Value in the Placebo Phase
  [Time Frame: 36 weeks] [Designated as safety issue: No]

  Subjects were assessed according to the United Parkinson's Disease Rating Scale UPDRS,(version 3;) Parts I and II are historical data and are designed to rate mentation, behavior and mood; Part III is done as a motor examination at the time of a visit. The UPDRS measures patient status on a scale 0, which is normal or none, to 4, which is severe or the worst scenario.

Enrollment: 1174
Study Start Date: November 2005
Study Completion Date: June 2009
Primary Completion Date: April 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: 1mg rasagiline 1mg early start active treatment arm (72 weeks active)followed by 1mg 36 week delayed start active treatment arm (36 weeks placebo followed by 36 weeks active)	Drug: Rasagiline Mesylate tablet, 1mg once daily
Experimental: 2mg rasagiline 2mg early start active treatment arm (72 weeks active)followed by 2mg 36 week delayed start active treatment arm (36 weeks placebo followed by 36 weeks active)	Drug: Rasagiline Mesylate tablet, 2mg once daily
Placebo Comparator: Placebo Each arm is followed by 36 weeks of placebo	Other: Placebo Placebo

Eligibility

Ages Eligible for Study: 30 Years to 80 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Men and women with idiopathic PD whose diagnosis is confirmed at screening, with at least two cardinal signs without any other known or suspected cause of parkinsonism. If tremor is not present, subjects must have unilateral onset and persistent asymmetry.
- Subjects with a diagnosis of early idiopathic PD of less than 1½ years duration from time of documented diagnosis.
- Subjects whose clinical condition at the time of enrollment does not require anti-PD treatment and will not require for the next 9 months.
- Willing and able to give informed consent.

Exclusion Criteria:

- Subjects younger than 30 or older than 80 years.
- Subjects with loss of postural reflexes.
- Subjects with UPDRS Tremor score of 3 or greater in any limb.
- Subjects with Hoehn &Yahr Stage III or greater at screening.
- Subjects with freezing while walking.
- Subjects with any of the following features that tend to exclude PD as the cause of Parkinsonism:
- History of repeated strokes with stepwise progression of Parkinsonian features
- History of repeated head injury or history of definite encephalitis
- Sustained remission
- Supranuclear gaze palsy
- Cerebellar signs
- Early severe autonomic involvement
- Babinski's sign
- Presence of a cerebral tumour or communicating hydrocephalus
- MPTP exposure
- Oculogyric crises
- Subjects who have had previous use of rasagiline or selegiline
- Subjects having used other anti-PD medication basis at any time prior to baseline

- Subjects having used other anti-PD medication (including anticholinergics) for less than 3 weeks during the 3 month period prior to baseline. (not including a single L-Dopa dose as part of L-Dopa test)
- Subjects having used any other anti-PD medication (including anticholinergics) for less than 3 weeks prior to the 3 month period preceding baseline whose anti-PD medication is intentionally ceased in order for the subject to enter the study.
- Subjects who have a clinically significant or unstable medical or surgical condition that may preclude safe and complete participation
- Hypertensive subjects whose BP is not well controlled according to the medical record or as observed during the week of home BP recording prior to baseline
- Subjects diagnosed with melanoma based on the screening dermatologic examination, or with a history of melanoma. Subjects with suspicious lesions at baseline who do not undergo biopsy
- Subjects with significant cognitive impairment as defined by MMSE score < 26
- Subjects with clinically significant psychiatric illness, including major depression [Beck Depression Inventory (short form) ≥15
- Subjects with a history of alcohol or substance abuse within the past 2 years
- Subjects who have taken any experimental medications within 60 days prior to baseline
- Subjects who have used coenzyme Q10 (in daily doses > 300 mg) within 120 days prior to baseline
- Subjects who have used sympathomimetics (including over-the-counter remedies - nasal or oral), dextromethorphan, pethidine or St. John's Wort within the 7 days prior to baseline
- Subjects who have used antidepressants within 42 days prior to baseline
- Subjects who have used ciprofloxacin, a potent CYP 1A2 inhibitor within 7 days prior to baseline
- Subjects who have used MAO inhibitors including reserpine or methyldopa within the three months prior to baseline, or treatment with an anti-emetic or antipsychotic medication with central dopamine antagonist activity within the six months prior to baseline
- Women who are not postmenopausal, surgically sterilized, or using adequate birth control [oral birth control pills, IUD, or a long acting injectable form of contraception; barrier methods alone (i.e., condom) are not sufficient]. Women of childbearing potential without a negative pregnancy test at screening. Nursing women

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT00256204

Sponsors and Collaborators

Teva Pharmaceutical Industries

Investigators

Study Director: Yoni Weiss, MD Teva Pharmaceutical Industries

More Information

Additional Information:

For more information about Teva Neuroscience EXIT

For more information about Parkinson's Disease EXIT

Unified Parkinson's Disease Rating Scale EXIT

No publications provided by Teva Pharmaceutical Industries

Additional publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Smith KM, Eyal E, Weintraub D; ADAGIO Investigators. Combined rasagiline and antidepressant use in Parkinson disease in the ADAGIO study: effects on nonmotor symptoms and tolerability. JAMA Neurol. 2015 Jan;72(1):88-95. doi: 10.1001/jamaneurol.2014.2472.

Rascol O, Fitzer-Attas CJ, Hauser R, Jankovic J, Lang A, Langston JW, Melamed E, Poewe W, Stocchi F, Tolosa E, Eyal E, Weiss YM, Olanow CW. A double-blind, delayed-start trial of rasagiline in Parkinson's disease (the ADAGIO study): prespecified and post-hoc analyses of the need for additional therapies, changes in UPDRS scores, and non-motor outcomes. Lancet Neurol. 2011 May;10(5):415-23. doi: 10.1016/S1474-4422(11)70073-4. Epub 2011 Apr 7. Erratum in: Lancet Neurol. 2012 Dec;11(12):1021.

Olanow CW, Rascol O, Hauser R, Feigin PD, Jankovic J, Lang A, Langston W, Melamed E, Poewe W, Stocchi F, Tolosa E; ADAGIO Study Investigators. A double-blind, delayed-start trial of rasagiline in Parkinson's disease. N Engl J Med. 2009 Sep 24;361(13):1268-78. doi: 10.1056/NEJMoa0809335. Erratum in: N Engl J Med. 2011 May 12;364(19):1882.

Responsible Party:	Teva Pharmaceutical Industries
ClinicalTrials.gov Identifier:	NCT00256204 History of Changes
Other Study ID Numbers:	**TVP-1012/500** (ADAGIO)
Study First Received:	November 16, 2005
Results First Received:	March 8, 2010
Last Updated:	January 10, 2012
Health Authority:	United States: Food and Drug Administration Canada: Health Canada

Keywords provided by Teva Pharmaceutical Industries:
Parkinson's
Rasagiline Mesylate

Additional relevant MeSH terms:

Parkinson Disease	Central Nervous System Agents
Basal Ganglia Diseases	Enzyme Inhibitors
Brain Diseases	Molecular Mechanisms of Pharmacological Action
Central Nervous System Diseases	Monoamine Oxidase Inhibitors
Movement Disorders	Neuroprotective Agents
Nervous System Diseases	Pharmacologic Actions
Neurodegenerative Diseases	Physiological Effects of Drugs
Parkinsonian Disorders	Protective Agents
Rasagiline	Therapeutic Uses

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Results First Received: March 8, 2010

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Parkinson's Disease
Interventions:	Drug: Rasagiline Mesylate Other: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
1mg Delayed Start	1mg Rasagiline tablet QD 36 week delayed start active treatment arms (36 weeks placebo followed by 36 weeks Rasagiline)
1mg Early Start	1mg Rasagiline tablet QD early start active treatment arm (72 weeks active)
2mg Delayed Start	2mg Rasagiline tablet QD 36 week delayed start active treatment arms (36 weeks placebo followed by 36 weeks Rasagiline)
2mg Early Start	2mg Rasagiline tablet QD early start active treatment arm (72 weeks active)

Participant Flow: Overall Study

	1mg Delayed Start	**1mg Early Start**	**2mg Delayed Start**	**2mg Early Start**
STARTED	**298**	**288**	**295**	**293**

COMPLETED	**231**	**238**	**241**	**244**
NOT COMPLETED	**67**	**50**	**54**	**49**
Adverse Event	**10**	**14**	**16**	**14**
Death	**0**	**1**	**0**	**0**
Lost to Follow-up	**1**	**1**	**1**	**2**
Protocol Violation	**1**	**0**	**2**	**1**
Physician Decision	**0**	**0**	**1**	**2**
Withdrawal by Subject	**17**	**6**	**7**	**5**
Need for additional prohibited treatment	**38**	**28**	**27**	**25**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
1mg Delayed Start	1mg Rasagiline tablet QD 36 week delayed start active treatment arms (36 weeks placebo followed by 36 weeks Rasagiline)
1mg Early Start	1mg Rasagiline tablet QD early start active treatment arm (72 weeks active)
2mg Early Start	2mg Rasagiline tablet QD early start active treatment arm (72 weeks active)
2mg Delayed Start	2mg Rasagiline tablet QD 36 week delayed start active treatment arms (36 weeks placebo followed by 36 weeks Rasagiline)
Total	Total of all reporting groups

Baseline Measures

	1mg Delayed Start	1mg Early Start	2mg Early Start	2mg Delayed Start	Total
Number of Participants [units: participants]	**298**	**288**	**293**	**295**	**1174**
Age [units: participants]					
<=18 years	**0**	**0**	**0**	**0**	**0**
Between 18 and 65 years	**175**	**163**	**169**	**173**	**680**
>=65 years	**123**	**125**	**124**	**122**	**494**
Age [units: years] Mean (Standard Deviation)	**61.9 (9.6)**	**62.4 (9.7)**	**62.3 (9.6)**	**62.4 (9.7)**	**62.2 (9.6)**
Gender [units: participants]					
Female	**113**	**113**	**118**	**113**	**457**
Male	**185**	**175**	**175**	**182**	**717**
Region of Enrollment [units: participants]					

United States	**102**	**91**	**94**	**98**	**385**
Portugal	**4**	**4**	**4**	**4**	**16**
Spain	**12**	**12**	**12**	**12**	**48**
Austria	**2**	**2**	**2**	**2**	**8**
Israel	**22**	**23**	**21**	**21**	**87**
United Kingdom	**7**	**7**	**9**	**8**	**31**
Italy	**24**	**25**	**28**	**25**	**102**
France	**11**	**11**	**12**	**14**	**48**
Hungary	**8**	**8**	**6**	**7**	**29**
Canada	**28**	**27**	**29**	**25**	**109**
Argentina	**17**	**17**	**16**	**18**	**68**
Romania	**25**	**24**	**25**	**24**	**98**
Germany	**27**	**28**	**26**	**28**	**109**
Netherlands	**9**	**9**	**9**	**9**	**36**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline [Time Frame: 12w, 24w, 36w, 42w, 48w, 54w, 60w, 66w, 72w]

Measure Type	Primary
Measure Title	Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline
Measure Description	The primary efficacy endpoint was defined as the change in Total UPDRS from Baseline. Subjects were assessed according to the United Parkinson's Disease Rating Scale (UPDRS,(version 3;) Parts I and II are historical data and are designed to rate mentation, behavior and mood; Part III is done as a motor examination at the time of a visit. The UPDRS measures patient status on a scale 0, which is normal or none, to 4, which is severe or the worst scenario.
Time Frame	12w, 24w, 36w, 42w, 48w, 54w, 60w, 66w, 72w
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
1mg Delayed Start	1mg Rasagiline tablet QD 36 week delayed start active treatment arms (36 weeks placebo followed by 36 weeks Rasagiline)
1mg Early Start	1mg Rasagiline tablet QD early start active treatment arm (72 weeks active)
2mg Early Start	2mg Rasagiline tablet QD early start active treatment arm (72 weeks active)
2mg Delayed Start	2mg Rasagiline tablet QD 36 week delayed start active treatment arms (36 weeks placebo followed by 36 weeks Rasagiline)

Measured Values

	1mg Delayed Start	1mg Early Start	2mg Early Start	2mg Delayed Start
Number of Participants Analyzed [units: participants]	**298**	**288**	**293**	**295**
Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline [units: Scores on a scale] Mean (Standard Deviation)				
Week 12	**0.9 (4.9)**	**-1.2 (5.6)**	**-0.7 (4.8)**	**0.7 (5.6)**
Week 24	**3.0 (6.5)**	**-1.1 (5.6)**	**-0.5 (5.6)**	**2.2 (6.5)**
Week 36	**3.7 (7.2)**	**0.6 (5.9)**	**0.8 (6.5)**	**3.0 (6.9)**
Week 42	**2.4 (7.4)**	**0.2 (6.7)**	**0.4 (7.2)**	**1.7 (6.6)**
Week 48	**1.9 (6.9)**	**0.7 (7.0)**	**0.5 (7.1)**	**1.4 (6.8)**
Week 54	**1.9 (7.3)**	**0.7 (7.1)**	**0.8 (7.2)**	**1.1 (7.0)**
Week 60	**1.9 (7.5)**	**1.1 (7.3)**	**1.2 (7.9)**	**1.6 (7.4)**
Week 66	**2.5 (8.1)**	**1.5 (7.7)**	**1.5 (8.0)**	**2.0 (8.2)**
Week 72	**3.3 (8.9)**	**1.9 (8.1)**	**2.2 (8.1)**	**2.3 (7.8)**

Statistical Analysis 1 for Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline

Groups [1]	1mg Delayed Start vs. 1mg Early Start vs. 2mg Delayed Start
Method [2]	Repeated Measures Mixed Linear Model
P Value [3]	0.0133

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Hypothesis #1: Slopes Superiority of 1mg Rasagiline over Placebo in the PC Phase Where slope is the model estimate of the change from baseline in total UPDRS per week. In this analysis, all available post-baseline observations in the PC Phase of the trial are analyzed (ITT efficacy data analysis set, weeks 12, 24 and 36). The placebo groups for rasagiline 1mg (delayed-start) and 2mg (delayed-start)are combined to one placebo group.
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 2 for Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline

Groups [1]	1mg Delayed Start vs. 2mg Early Start vs. 2mg Delayed Start
Method [2]	Repeated Measures Mixed Linear Model
P Value [3]	0.0001

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Hypothesis #1: Slopes Superiority of 2mg Rasagiline over Placebo in the PC Phase Where slope is the model estimate of the change from baseline in total UPDRS per week. In this analysis, all available post-baseline observations in the PC Phase of the trial are analyzed (ITT efficacy data analysis set, weeks 12, 24 and 36). The placebo groups for rasagiline 1mg (delayed-start)and 2mg (delayed-start) are combined to one placebo group.

[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.

Statistical Analysis 3 for Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline

Groups [1]	1mg Delayed Start vs. 1mg Early Start
Method [2]	Repeated Measures
P Value [3]	0.0250

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Hypothesis #2: Superiority of Early over Delayed Start at Week 72 In this analysis, observations of subjects entering the active phase with at least 24 weeks of treatment during the PC Phase and at least one available Total UPDRS measurement during the active-treatment phase from weeks 48, 54, 60, 66 or 72, are analyzed (ACTE data analysis set).
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The analysis was performed on separate datasets and not on the combined dataset as was pre-specified to account for unexpected interactions of dose level by baseline UPDRS and of dose level by center .

Statistical Analysis 4 for Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline

Groups [1]	2mg Early Start vs. 2mg Delayed Start
Method [2]	Repeated Measures
P Value [3]	0.6028

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Hypothesis #2:Superiority of Early over Delayed Start at Week 72 In this analysis, observations of subjects entering the active phase with at least 24 weeks of treatment during the PC Phase and at least one available Total UPDRS measurement during the active-treatment phase from weeks 48, 54, 60, 66 or 72, are analyzed (ACTE data analysis set.)
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	The analysis was performed on separate datasets and not on the combined dataset as was pre-specified to account for unexpected interactions of dose level by baseline UPDRS and of dose level by center

Statistical Analysis 5 for Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline

Groups [1]	1mg Delayed Start vs. 1mg Early Start
Non-Inferiority/Equivalence Test [2]	Yes
Slope [3]	0.000
90% Confidence Interval	-0.036 to 0.036

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Hypothesis #3: Slopes Non-Inferiority of Early Start over Delayed Start in the Active Phase.

	Where slope is the model estimate of the change from baseline in total UPDRS per week. In this analysis, observations of all subjects entering the active phase with at least 24 weeks of treatment during the PC Phase and at least one available Total UPDRS measurement during the active treatment phase from weeks 48, 54, 60, 66 or 72, are analyzed (ACTE data analysis set).
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Non-Inf Test for difference in slopes between treatment groups. One sided 95% CI calculated for difference between slopes of the 1mg early-start group and the 1mg delayed-start group. The inferiority null hypothesis of the early-start group slope over delayed-start group slope is rejected, if the upper limit of one sided 95% CI for difference in slopes does not cross non-inferiority margin of 0.15 UPDRS points per week.
[3]	Other relevant estimation information:
	No text entered.

Statistical Analysis 6 for Change in Total Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline

Groups [1]	2mg Early Start vs. 2mg Delayed Start
Non-Inferiority/Equivalence Test [2]	Yes
Slope [3]	0.029
90% Confidence Interval	-0.005 to 0.062

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Hypothesis #3: Slopes Non-Inferiority of Early Start over Delayed Start in the Active Phase. Where slope is the model estimate of the change from baseline in total UPDRS per week. In this analysis, observations of all subjects entering the active phase with at least 24 weeks of treatment during the PC Phase and at least one available Total UPDRS measurement during the active treatment phase from weeks 48, 54, 60, 66 or 72, are analyzed (ACTE data analysis set).
[2]	Details of power calculation, definition of non-inferiority margin, and other key parameters:
	Non-Inf Test for difference in slopes between treatment groups. One sided 95% CI calculated for difference between slopes of the 2mg early-start group and the 2mg delayed-start group. The inferiority null hypothesis of the early-start group slope over delayed-start group slope is rejected, if the upper limit of one sided 95% CI for difference in slopes does not cross non-inferiority margin of 0.15 UPDRS points per week.
[3]	Other relevant estimation information:
	No text entered.

2. Secondary: Change in Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline to Last Observed Value in the Placebo Phase [Time Frame: 36 weeks]

Measure Type	Secondary
Measure Title	Change in Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline to Last Observed Value in the Placebo Phase
Measure Description	Subjects were assessed according to the United Parkinson's Disease Rating Scale UPDRS,(version 3;) Parts I and II are historical data and are designed to rate mentation, behavior and mood; Part III is done as a motor examination at the time of a visit. The UPDRS measures patient status on a scale 0, which is normal or none, to 4, which is severe or the worst scenario.
Time Frame	36 weeks
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
1mg Delayed Start	+ 2 mg Delayed Start: 36 week combined placebo group.
1mg Early Start	1mg early start active treatment arm (72 weeks active)
2mg Early Start	2mg early start active treatment arm (72 weeks active)
2mg Delayed Start	+1mg Delayed Start: see 1st column

Measured Values

	1mg Delayed Start	1mg Early Start	2mg Early Start	2mg Delayed Start
Number of Participants Analyzed [units: participants]	**588**	**286**	**290**	**0**
Change in Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline to Last Observed Value in the Placebo Phase [units: Scores on a scale] Mean (Standard Deviation)	**3.9 (7.2)**	**1.0 (6.0)**	**0.8 (6.5)**	

Statistical Analysis 1 for Change in Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline to Last Observed Value in the Placebo Phase

Groups [1]	1mg Delayed Start vs. 1mg Early Start vs. 2mg Delayed Start
Method [2]	ANCOVA
P Value [3]	<0.0001
Mean Difference (Final Values) [4]	-3.005
95% Confidence Interval	-3.857 to -2.153

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The adjusted means of the changes in Total UPDRS from baseline to LOV in the placebo-controlled phase, observed in the 1 mg and 2 mg rasagiline early-start groups are compared (two contrasts) to the combined placebo group (1 mg and 2 mg rasagiline delayed-start groups), by applying an Analysis of Covariance model. The model includes treatment group, center and baseline Total UPDRS as covariates. For this analysis, both delayed start arms are pooled as a 'placebo arm'
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change in Unified Parkinson's Disease Rating Scale (UPDRS) Score From Baseline to Last Observed Value in the Placebo Phase

Groups [1]	1mg Delayed Start vs. 2mg Early Start vs. 2mg Delayed Start
Method [2]	ANCOVA
P Value [3]	<0.0001
Mean Difference (Final Values) [4]	-3.154
95% Confidence Interval	-4.004 to -2.305

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	The adjusted means of the changes in Total UPDRS from baseline to LOV in the placebo-controlled phase, observed in the 1 mg and 2 mg rasagiline early-start groups are compared (two contrasts) to the combined placebo group (1 mg and 2 mg rasagiline delayed-start groups), by applying an Analysis of Covariance model. The model includes treatment group, center and baseline Total UPDRS as covariates. For this analysis, both delayed start arms are pooled as a 'placebo arm'
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[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	2 years, 6 months
Additional Description	Each Delayed Start arm was preceded by 36 weeks placebo followed by 36 weeks Rasagiline either 1mg or 2mg; therefore, the placebo groups were combined into one group for the placebo analysis.

Reporting Groups

	Description
Placebo Combined Group	1mg & 2mg combined placebo group includes those patients in 1mg Delayed start and the 2mg Delayed start arms who received placebo for the first 36 weeks.
1mg Active Treatment	1mg Active & 1mg Delayed. This group includes those patients who received 1mg Rasagiline in both the early start active treatment arm (72 weeks active)and those patients who transitioned to active treatment in the 1mg Delayed start treatment arm (36 weeks active treatment)
2mg Active Treatment	2mg Active & 2mg Delayed. This group includes those patients who received 2mg Rasagiline in both the early start active treatment arm (72 weeks active)and those patients who transitioned to active treatment in the 2mg Delayed start treatment arm (36 weeks active treatment)

Serious Adverse Events

	Placebo Combined Group	1mg Active Treatment	2mg Active Treatment
Total, serious adverse events			
# participants affected / at risk	**22/593 (3.71%)**	**37/288 (12.85%)**	**44/293 (15.02%)**
Cardiac disorders			
Coronary Artery Disease			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Cardiac failure			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Angina Pectoris			
# participants affected / at risk	**1/593 (0.17%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**1**	**1**	**0**

Myocardial Infarction			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**2/293 (0.68%)**
# events	**1**	**0**	**2**
Atrial Fibrilation			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**1**	**0**	**1**
Atrial Flutter			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Cardiac Failure Congestive			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Myocardial Ischaemia			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Tachycardia			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Ear and labyrinth disorders			
Vertigo			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Eye disorders			
Vitreous Haemorrhage			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Eyelid Ptosis			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Cataract			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Retinal Vein Occlusion			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Gastrointestinal disorders			
Abdominal Pain			
# participants affected / at risk	**1/593 (0.17%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**1**	**1**	**0**
Abdominal Pain Lower			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Parasthesia Oral			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Duodenal Ulcer Haemorrhage			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Gastritis			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**

Heus			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Inguinal Hernia			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Gastrointestinal Haemorrhage			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
General disorders			
Pyrexia			
# participants affected / at risk	**0/593 (0.00%)**	**2/288 (0.69%)**	**0/293 (0.00%)**
# events	**0**	**2**	**0**
Chest Discomfort			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Chest pain			
# participants affected / at risk	**0/593 (0.00%)**	**4/288 (1.39%)**	**0/293 (0.00%)**
# events	**0**	**4**	**0**
Non-Cardiac Chest Pain			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Malaise			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Immune system disorders			
Drug Hypersensitivity			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**2**	**0**
Infections and infestations			
Appendicitis			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Cellulitis			
# participants affected / at risk	**1/593 (0.17%)**	**1/288 (0.35%)**	**1/293 (0.34%)**
# events	**1**	**1**	**1**
Labyrinthitis			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Bronchitis			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Pneumonia			
# participants affected / at risk	**1/593 (0.17%)**	**2/288 (0.69%)**	**1/293 (0.34%)**
# events	**1**	**2**	**1**
Urosepsis			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Laryngitis			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**

Diverticulitis			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Rectal Abscess			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Peridiverticular Abscess			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Lower respiratory Tract Infection			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Erysipelas			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Injury, poisoning and procedural complications			
Femur Fracture			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Hip Fracture			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**1/293 (0.34%)**
# events	**0**	**1**	**1**
Fall			
# participants affected / at risk	**1/593 (0.17%)**	**2/288 (0.69%)**	**0/293 (0.00%)**
# events	**1**	**2**	**0**
Femoral Neck Fracture			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Investigations			
Arteriogram Coronary Abnormal			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Metabolism and nutrition disorders			
Hypokalaemia			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Hyponatraemia			
# participants affected / at risk	**1/593 (0.17%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**1**	**1**	**0**
Dehydration			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**2/293 (0.68%)**
# events	**0**	**0**	**2**
Musculoskeletal and connective tissue disorders			
Myalgia			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Muscle Hemorrhage			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Osteoarthritis			

# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	3/293 (1.02%)
# events	0	0	3
Back Pain			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	1/293 (0.34%)
# events	0	1	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Diffuse Large B-Cell Lymphoma			
# participants affected / at risk	1/593 (0.17%)	0/288 (0.00%)	0/293 (0.00%)
# events	1	0	0
Thyroid Neoplasm			
# participants affected / at risk	1/593 (0.17%)	0/288 (0.00%)	0/293 (0.00%)
# events	1	0	0
Endometrial Cancer Stage I			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Lung Adenocarcinoma Metastic			
# participants affected / at risk	1/593 (0.17%)	0/288 (0.00%)	0/293 (0.00%)
# events	1	0	0
Benign Laryngeal Neoplasm			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Rectal cancer Metastic			
# participants affected / at risk	1/593 (0.17%)	0/288 (0.00%)	0/293 (0.00%)
# events	1	0	0
Breast cancer			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Colon Cancer			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Squamous Cell Carcinoma			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Ovarian Epithelial Cancer Metastatic			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Prostrate Cancer			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	1/293 (0.34%)
# events	0	1	1
Renal cancer			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Basal Cell Carcinoma			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	1/293 (0.34%)
# events	0	2	1
Nervous system disorders			
Cerebral Haemorrhage			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Subarachnoid Haemorrhage			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)

# events	0	0	1
Lacunar Infarction			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Syncope			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Akinesia			
# participants affected / at risk	1/593 (0.17%)	0/288 (0.00%)	0/293 (0.00%)
# events	1	0	0
Headache			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Hydrocephalus			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Parkinson's Disease			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Carotid Artery Stenosis			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Loss of Consciousness			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Sciatica			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Aphasia			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Transient Ischaemic Attack			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Psychiatric disorders			
Major Depression			
# participants affected / at risk	1/593 (0.17%)	0/288 (0.00%)	0/293 (0.00%)
# events	1	0	0
Alcohol Abuse			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Neurosis			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Hallucination, Visual			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Suicidal Ideation			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Renal and urinary disorders			

Renal Colic			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Nephrolithiasis			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Reproductive system and breast disorders			
Laryngeal Leukoplakia			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Atelectasis			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Colpocele			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**1**	**0**	**1**
Pulmonary Embolism			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Pulmonary Infarction			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Skin and subcutaneous tissue disorders			
Hypoaesthesia Facial			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**2**	**0**	**0**
Rash			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Surgical and medical procedures			
Coronary Artery Bypass			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Cardioversion			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**0/293 (0.00%)**
# events	**0**	**1**	**0**
Open reduction of fracture			
# participants affected / at risk	**1/593 (0.17%)**	**0/288 (0.00%)**	**0/293 (0.00%)**
# events	**1**	**0**	**0**
Incisional Hernia Repair			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**
Inguinal Hernia Repair			
# participants affected / at risk	**0/593 (0.00%)**	**1/288 (0.35%)**	**1/293 (0.34%)**
# events	**0**	**1**	**1**
Knee Operation			

# participants affected / at risk	1/593 (0.17%)	0/288 (0.00%)	0/293 (0.00%)
# events	1	0	0
Colon Polypectomy			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Hysterectomy			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Abdominal Operation			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Arterial Stent Insertion			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Coronary Angioplasty			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Bone operation			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Hip Arthroplasty			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	1/293 (0.34%)
# events	0	1	1
Hip Surgery			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Knee Arthroplasty			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	2/293 (0.68%)
# events	0	0	2
Cataract Operation			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Transurethral Prostatectomy			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Vascular disorders			
Hypotension			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1
Aortic Aneurysm			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	1/293 (0.34%)
# events	0	1	1
Aortic Aneurysm Rupture			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Deep Vein Thrombosis			
# participants affected / at risk	0/593 (0.00%)	1/288 (0.35%)	0/293 (0.00%)
# events	0	1	0
Thrombophlebitis			
# participants affected / at risk	0/593 (0.00%)	0/288 (0.00%)	1/293 (0.34%)
# events	0	0	1

Hypertension			
# participants affected / at risk	**0/593 (0.00%)**	**0/288 (0.00%)**	**1/293 (0.34%)**
# events	**0**	**0**	**1**

Other Adverse Events

Hide Other Adverse Events

Time Frame	2 years, 6 months
Additional Description	Each Delayed Start arm was preceded by 36 weeks placebo followed by 36 weeks Rasagiline either 1mg or 2mg; therefore, the placebo groups were combined into one group for the placebo analysis.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Placebo Combined Group	1mg & 2mg combined placebo group includes those patients in 1mg Delayed start and the 2mg Delayed start arms who received placebo for the first 36 weeks.
1mg Active Treatment	1mg Active & 1mg Delayed. This group includes those patients who received 1mg Rasagiline in both the early start active treatment arm (72 weeks active)and those patients who transitioned to active treatment in the 1mg Delayed start treatment arm (36 weeks active treatment)
2mg Active Treatment	2mg Active & 2mg Delayed. This group includes those patients who received 2mg Rasagiline in both the early start active treatment arm (72 weeks active)and those patients who transitioned to active treatment in the 2mg Delayed start treatment arm (36 weeks active treatment)

Other Adverse Events

	Placebo Combined Group	**1mg Active Treatment**	**2mg Active Treatment**
Total, other (not including serious) adverse events			
# participants affected / at risk	**82/593 (13.83%)**	**40/288 (13.89%)**	**34/293 (11.60%)**
General disorders			
Fatigue			
# participants affected / at risk	**17/593 (2.87%)**	**17/288 (5.90%)**	**10/293 (3.41%)**
# events	**18**	**18**	**10**
Musculoskeletal and connective tissue disorders			
Back Pain			
# participants affected / at risk	**32/593 (5.40%)**	**14/288 (4.86%)**	**15/293 (5.12%)**
# events	**34**	**14**	**15**
Nervous system disorders			
Headache			
# participants affected / at risk	**37/593 (6.24%)**	**14/288 (4.86%)**	**15/293 (5.12%)**
# events	**39**	**15**	**15**

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:** Should the Oversight Committee wish to publish the results of this study, the Oversight Committee agrees to provide Teva with a manuscript for review 60 days prior to submission for publication. Teva retains the right to delete from the manuscript confidential information and to object to suggested publication and/or its timing (at the sole discretion of Teva).

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No publications provided by Teva Pharmaceutical Industries

Publications automatically indexed to this study:

Smith KM, Eyal E, Weintraub D; ADAGIO Investigators. Combined rasagiline and antidepressant use in Parkinson disease in the ADAGIO study: effects on nonmotor symptoms and tolerability. JAMA Neurol. 2015 Jan;72(1):88-95. doi: 10.1001/jamaneurol.2014.2472.

Rascol O, Fitzer-Attas CJ, Hauser R, Jankovic J, Lang A, Langston JW, Melamed E, Poewe W, Stocchi F, Tolosa E, Eyal E, Weiss YM, Olanow CW. A double-blind, delayed-start trial of rasagiline in Parkinson's disease (the ADAGIO study): prespecified and post-hoc analyses of the need for additional therapies, changes in UPDRS scores, and non-motor outcomes. Lancet Neurol. 2011 May;10(5):415-23. doi: 10.1016/S1474-4422(11)70073-4. Epub 2011 Apr 7. Erratum in: Lancet Neurol. 2012 Dec;11(12):1021.

Olanow CW, Rascol O, Hauser R, Feigin PD, Jankovic J, Lang A, Langston W, Melamed E, Poewe W, Stocchi F, Tolosa E; ADAGIO Study Investigators. A double-blind, delayed-start trial of rasagiline in Parkinson's disease. N Engl J Med. 2009 Sep 24;361(13):1268-78. doi: 10.1056/NEJMoa0809335. Erratum in: N Engl J Med. 2011 May 12;364(19):1882.

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