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Trial record **1 of 1** for: CENA713D2340

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Comparative Efficacy, Safety, and Tolerability of Rivastigmine 10 and 15 cm^2 Patch in Patients With Alzheimer's Disease (AD) Showing Cognitive Decline

This study has been completed.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00506415

First received: July 20, 2007
Last updated: September 17, 2012
Last verified: September 2012
History of Changes

Results First Received: May 1, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator); Primary Purpose: Treatment
Condition:	Alzheimer Disease
Interventions:	Drug: Rivastigmine 5 cm^2 Drug: Rivastigmine 10 cm^2 Drug: Rivastigmine 15 cm^2 Drug: Placebo to 15 cm^2 patch

	Drug: Placebo to 10 cm^2 patch

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
1,584 participants were enrolled, 1582 received study drug during the initial open label period; of these, 567 were qualified to enter a double blind randomized period.

Reporting Groups

	Description
Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	Rivastigmine 5 cm^2 transdermal patch once a day during the first 4 weeks of open label treatment followed by rivastigmine 10 cm^2 transdermal patch once a day from week 4 to week 24, 36 or 48.
Double Blind: Rivastigmine (10 cm^2)	Rivastigmine transdermal patch 10 cm^2 and placebo to rivastigmine 15 cm^2 once daily for 48 weeks during the double blind period.
Double Blind: Rivastigmine (15 cm^2)	Rivastigmine transdermal patch 15 cm^2 and placebo to rivastigmine 10 cm^2 once daily for 48 weeks during double blind period.
Extended Open Label (10 cm^2)	Rivastigmine 10 cm^2 transdermal patch once a day during 48 weeks (from week 48 to week 96) open label treatment.

Participant Flow for 3 periods

Period 1: Initial Open Label (Maximum 48 Weeks)

	Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	Double Blind: Rivastigmine (10 cm^2)	Double Blind: Rivastigmine (15 cm^2)	Extended Open Label (10 cm^2)
STARTED	**1584** [1]	**0**	**0**	**0**

Exposed to Study Drug	**1582**	**0**	**0**	**0**
COMPLETED	**1085**	**0**	**0**	**0**
NOT COMPLETED	**499**	**0**	**0**	**0**
Adverse Event	**272**	**0**	**0**	**0**
Abnormal laboratory value	**1**	**0**	**0**	**0**
Abnormal test procedure results	**1**	**0**	**0**	**0**
Unsatisfactory therapeutic effect	**58**	**0**	**0**	**0**
Withdrawal by Subject	**88**	**0**	**0**	**0**
Lost to Follow-up	**22**	**0**	**0**	**0**
Administrative problem	**7**	**0**	**0**	**0**
Death	**22**	**0**	**0**	**0**
Protocol Violation	**28**	**0**	**0**	**0**

[1] Enrolled patients.

Period 2: Double Blind (Maximum 48 Weeks)

	Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	Double Blind: Rivastigmine (10 cm^2)	Double Blind: Rivastigmine (15 cm^2)	Extended Open Label (10 cm^2)
STARTED	**0**	**286** [1]	**280**	**0**
COMPLETED	**0**	**203**	**207**	**0**
NOT COMPLETED	**0**	**83**	**73**	**0**
Adverse Event	**0**	**33**	**28**	**0**
Death	**0**	**5**	**3**	**0**
Unsatisfactory therapeutic effect	**0**	**13**	**13**	**0**

Protocol Violation	**0**	**5**	**3**	**0**
Lost to Follow-up	**0**	**4**	**6**	**0**
Withdrawal by Subject	**0**	**20**	**17**	**0**
Administrative problems	**0**	**3**	**2**	**0**
Condition no longer requires study drug	**0**	**0**	**1**	**0**

[1] 1 patient was randomized in error and did not receive study drug, hence excluded from this arm.

Period 3: Extended Open Label (Maximum 48 Weeks)

	Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	Double Blind: Rivastigmine (10 cm^2)	Double Blind: Rivastigmine (15 cm^2)	Extended Open Label (10 cm^2)
STARTED	**0**	**0**	**0**	**457** [1]
COMPLETED	**0**	**0**	**0**	**395**
NOT COMPLETED	**0**	**0**	**0**	**62**
Administrative problems	**0**	**0**	**0**	**4**
Adverse Event	**0**	**0**	**0**	**18**
Lost to Follow-up	**0**	**0**	**0**	**8**
Withdrawal by Subject	**0**	**0**	**0**	**14**
Protocol Violation	**0**	**0**	**0**	**5**
Unsatisfactory therapeutic effect	**0**	**0**	**0**	**6**
Death	**0**	**0**	**0**	**7**

[1] Two participants did not receive study drug, hence excluded from this arm.

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
Total Patients	Total number of patients enrolled in the initial open label period that may have been randomized in the double blind period or may have continued in the extended open label period.

Baseline Measures

	Total Patients
Number of Participants [units: participants]	**1584**
Age [units: years] Mean (Standard Deviation)	**74.93 (7.131)**
Gender [units: participants]	
Female	**992**
Male	**592**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline in Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) Subscale at Week 48 of Double Blind Period [Time Frame: Baseline and week 48 of double blind period]

Measure Type	Primary
Measure Title	Change From Baseline in Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) Subscale at Week 48 of Double Blind Period
Measure Description	The Alzheimer's Disease Assessment Scale-Cognitive (ADAS-cog) subscale comprises 11 items summed to a total score ranging from 0 to 70, with lower scores indicating less severe impairment. A negative change indicates an improvement from baseline.
Time Frame	Baseline and week 48 of double blind period
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.
Intent to treat population double blind (ITT-DB): included all randomized patients who received at least 1 dose of double blind study drug, and had at least 1 post-randomization assessment for both co-primary efficacy variables: Alzheimer's Disease Assessment Scale-Cognitive and Disease Cooperative Study-Instrumental Activities of Daily Living.

Reporting Groups

	Description
Double Blind: Rivastigmine (10 cm^2)	Rivastigmine transdermal patch 10 cm^2 and placebo to rivastigmine 15 cm^2 once daily for 48 weeks during the double blind period.
Double Blind: Rivastigmine (15 cm^2)	Rivastigmine transdermal patch 15 cm^2 and placebo to rivastigmine 10 cm^2 once daily for 48 weeks during double blind period.

Measured Values

	Double Blind: Rivastigmine (10 cm^2)	**Double Blind: Rivastigmine (15 cm^2)**
Number of Participants Analyzed [units: participants]	**268**	**264**
Change From Baseline in Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) Subscale at Week 48 of Double Blind Period [units: units on a scale]	**4.9 (7.49)**	**4.1 (8.00)**

Mean (Standard Deviation)		

No statistical analysis provided for Change From Baseline in Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) Subscale at Week 48 of Double Blind Period

2. Primary: Change in Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) Subscale Score From Baseline to Week 48 of Double Blind Period [Time Frame: Baseline and week 48 of double blind period]

Measure Type	Primary
Measure Title	Change in Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) Subscale Score From Baseline to Week 48 of Double Blind Period
Measure Description	The Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) is a 16 item subscale of the caregiver-based ADCS-IADL scale, developed for the use in dementia studies. The ADCS-IADL total score ranges from 0 to 56, with higher scores indicating less severe impairment. A positive change indicates an improvement from baseline.
Time Frame	Baseline and week 48 of double blind period
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.
Intent to treat population double blind (ITT-DB): included all randomized patients who received at least 1 dose of double blind study drug, and had at least 1 post-randomization assessment for both co-primary efficacy variables: Alzheimer's Disease Assessment Scale-Cognitive and Disease Cooperative Study-Instrumental Activities of Daily Living.

Reporting Groups

	Description
Double Blind: Rivastigmine (10 cm^2)	Rivastigmine transdermal patch 10 cm^2 and placebo to rivastigmine 15 cm^2 once daily for 48 weeks during the double blind period.
Double Blind: Rivastigmine (15 cm^2)	Rivastigmine transdermal patch 15 cm^2 and placebo to rivastigmine 10 cm^2 once daily for 48 weeks during double blind period.

Measured Values

	Double Blind: Rivastigmine (10 cm^2)	Double Blind: Rivastigmine (15 cm^2)
Number of Participants Analyzed **[units: participants]**	**271**	**265**
Change in Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) Subscale Score From Baseline to Week 48 of Double Blind Period **[units: units on a scale]** **Mean (Standard Deviation)**	**-6.2 (8.78)**	**-4.4 (8.21)**

No statistical analysis provided for Change in Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) Subscale Score From Baseline to Week 48 of Double Blind Period

3. Secondary: Time to Functional Decline as Measured by Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) Subscale During the Double Blind Period [Time Frame: 390 days was the maximum]

Measure Type	Secondary
Measure Title	Time to Functional Decline as Measured by Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) Subscale During the Double Blind Period
Measure Description	Functional decline was defined by either an at least 1 point decrease in the Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) subscale score in a visit and confirmed by the following visit/assessment or at least 2 points decrease from the double blind randomization baseline.
Time Frame	390 days was the maximum
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.

Intent to treat population double blind (ITT-DB): included all randomized patients who received at least 1 dose of double blind study drug, and had at least 1 post-randomization assessment for both co-primary efficacy variables: Alzheimer's Disease Assessment Scale-Cognitive and Disease Cooperative Study-Instrumental Activities of Daily Living.

Reporting Groups

	Description
Double Blind: Rivastigmine (10 cm^2)	Rivastigmine transdermal patch 10 cm^2 and placebo to rivastigmine 15 cm^2 once daily for 48 weeks during the double blind period.
Double Blind: Rivastigmine (15 cm^2)	Rivastigmine transdermal patch 15 cm^2 and placebo to rivastigmine 10 cm^2 once daily for 48 weeks during double blind period.

Measured Values

	Double Blind: Rivastigmine (10 cm^2)	Double Blind: Rivastigmine (15 cm^2)
Number of Participants Analyzed **[units: participants]**	**271**	**265**
Time to Functional Decline as Measured by Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) Subscale During the Double Blind Period **[units: Time in days]** **Median (95% Confidence Interval)**	**90 (85 to 113)**	**91 (85 to 113)**

No statistical analysis provided for Time to Functional Decline as Measured by Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-IADL) Subscale During the Double Blind Period

4. Secondary: Change in Attention and Executive Function as Assessed by the Trail Making Test (Part A) at Week 48 of the Double Blind Period [Time Frame: Baseline and week 48 of double blind period]

Measure Type	Secondary
Measure Title	Change in Attention and Executive Function as Assessed by the Trail Making Test (Part A) at Week 48 of the Double Blind Period

Measure Description	Change from baseline to week 48 in total time to perform Trail Making Test (TMT) part A. This test provides information on visual search, scanning, speed of processing, mental flexibility, and executive functions. The TMT part A requires an individual to draw lines sequentially connecting 25 encircled numbers distributed on a sheet of paper. The score represents the amount of time required to complete the task. Total values for TMT part A range between 0 and 300 seconds. A negative change indicates an improvement from baseline.
Time Frame	Baseline and week 48 of double blind period
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.
Intent to treat population (ITT-DB): included all randomized patients with an assessment at baseline and week 48 who received at least 1 dose of double blind study drug, and had at least 1 post-randomization assessment for both co-primary efficacy variables (ADAS-cog and ADCS-IADL).

Reporting Groups

	Description
Double Blind: Rivastigmine (10 cm^2)	Rivastigmine transdermal patch 10 cm^2 and placebo to rivastigmine 15 cm^2 once daily for 48 weeks during the double blind period.
Double Blind: Rivastigmine (15 cm^2)	Rivastigmine transdermal patch 15 cm^2 and placebo to rivastigmine 10 cm^2 once daily for 48 weeks during double blind period.

Measured Values

	Double Blind: Rivastigmine (10 cm^2)	**Double Blind: Rivastigmine (15 cm^2)**
Number of Participants Analyzed **[units: participants]**	**258**	**254**
Change in Attention and Executive Function as Assessed by the Trail Making Test (Part A) at Week 48 of the Double Blind Period **[units: Time in seconds]** **Mean (Standard Deviation)**	**18.2 (62.57)**	**16.3 (66.09)**

No statistical analysis provided for Change in Attention and Executive Function as Assessed by the Trail Making Test (Part A) at Week 48 of the Double Blind Period

5. Secondary: Change in Attention and Executive Function as Assessed by the Trail Making Test (Part B) at Week 48 of Double Blind Period [Time Frame: Baseline and week 48 of double blind period]

Measure Type	Secondary
Measure Title	Change in Attention and Executive Function as Assessed by the Trail Making Test (Part B) at Week 48 of Double Blind Period
Measure Description	Change from baseline to week 48 in total time to perform Trail Making Test (TMT) part B. This test provides information on visual search, scanning, speed of processing, mental flexibility, and executive functions. TMT has two parts: Part A requires an individual to draw lines sequentially connecting 25 encircled numbers distributed on a sheet of paper. Task requirements are similar for TMT-Part B except the person must alternate between numbers and letters. Total values for TMT part B range between 0 and 420 seconds. A negative change from baseline indicates an improvement in condition.
Time Frame	Baseline and week 48 of double blind period
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.
Intent to treat population (ITT-DB): included all randomized patients with an assessment at baseline and week 48 who received at least 1 dose of double blind study drug, and had at least 1 post-randomization assessment for both co-primary efficacy variables (ADAS-cog, ADCS-IADL).

Reporting Groups

	Description
Double Blind: Rivastigmine (15 cm^2)	Rivastigmine transdermal patch 15 cm^2 and placebo to rivastigmine 10 cm^2 once daily for 48 weeks during the double blind period.
Double Blind: Rivastigmine (10 cm^2)	Rivastigmine transdermal patch 10 cm^2 and placebo to rivastigmine 15 cm^2 once daily for 48 weeks during the double blind period.

Measured Values

	Double Blind: Rivastigmine (15 cm^2)	Double Blind: Rivastigmine (10 cm^2)
Number of Participants Analyzed [units: participants]	**235**	**236**
Change in Attention and Executive Function as Assessed by the Trail Making Test (Part B) at Week 48 of Double Blind Period [units: Time in seconds] Mean (Standard Deviation)	**9.3 (68.80)**	**5.8 (65.38)**

No statistical analysis provided for Change in Attention and Executive Function as Assessed by the Trail Making Test (Part B) at Week 48 of Double Blind Period

6. Secondary: Change From Baseline in Neuropsychiatric Inventory (NPI)-10 Score at Week 48 of Double Blind Period [Time Frame: Baseline and week 48 of double blind period]

Measure Type	Secondary
Measure Title	Change From Baseline in Neuropsychiatric Inventory (NPI)-10 Score at Week 48 of Double Blind Period
Measure Description	Change from baseline to week 48 as assessed by the Neuropsychiatric Inventory (NPI)-10 total score. The scale consists of 10 domains that are rated for both frequency (range 1-4) and severity (range 1-3). A composite score for each domain is calculated (frequency x severity) which ranges from 1 to 12. There is a leading question for each item. If the symptom is not present then the frequency, severity and distress scores are not completed. In this case the score is 0 for the item. The sum of the composite scores yields the NPI-10 total score (range 0-120). A negative change in score indicates an improvement from baseline (symptom reduction).
Time Frame	Baseline and week 48 of double blind period
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.
Intent to treat population double blind (ITT-DB): included all randomized patients with an assessment at baseline and week 48, who received at least 1 dose of double blind study drug, and had at least 1 post-randomization assessment for both co-primary efficacy variables (ADAS-cog, ADCS-IADL).

Reporting Groups

	Description
Double Blind: Rivastigmine (10 cm^2)	Rivastigmine transdermal patch 10 cm^2 and placebo to rivastigmine 15 cm^2 once daily for 48 weeks during the double blind period.
Double Blind: Rivastigmine (15 cm^2)	Rivastigmine transdermal patch 15 cm^2 and placebo to rivastigmine 10 cm^2 once daily for 48 weeks during double blind period.

Measured Values

	Double Blind: Rivastigmine (10 cm^2)	Double Blind: Rivastigmine (15 cm^2)
Number of Participants Analyzed **[units: participants]**	**271**	**265**
Change From Baseline in Neuropsychiatric Inventory (NPI)-10 Score at Week 48 of Double Blind Period **[units: units on a scale]** **Mean (Standard Deviation)**	**0.9 (10.98)**	**1.4 (11.51)**

No statistical analysis provided for Change From Baseline in Neuropsychiatric Inventory (NPI)-10 Score at Week 48 of Double Blind Period

7. Secondary: Number of Patients With Adverse Events, Serious Adverse Events and Discontinuations Due to Adverse Events [Time Frame: 30 days after a maximum of 96 weeks treatment]

Measure Type	Secondary
Measure Title	Number of Patients With Adverse Events, Serious Adverse Events and Discontinuations Due to Adverse Events
Measure Description	No text entered.
Time Frame	30 days after a maximum of 96 weeks treatment
Safety Issue	Yes

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.
The safety set included all patients who received at least one dose of study medication and who had at least one post-baseline safety assessment.

Reporting Groups

	Description
Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	Rivastigmine 5 cm^2 transdermal patch once a day during the first 4 weeks of open label treatment followed by rivastigmine 10 cm^2 transdermal patch once a day from week 4 to week 24, 36 or 48.
Double Blind: Rivastigmine (10 cm^2)	Rivastigmine transdermal patch 10 cm^2 and placebo to rivastigmine 15 cm^2 once daily for 48 weeks during the double blind period.
Double Blind: Rivastigmine (15 cm^2)	Rivastigmine transdermal patch 15c m^2 and placebo to rivastigmine 10 cm^2 once daily for 48 weeks during double blind period.
Extended Open Label (10 cm^2)	Rivastigmine 10 cm^2 transdermal patch once a day during 48 weeks open label treatment running in parallel to the double blind period.

Measured Values

	Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	**Double Blind: Rivastigmine (10 cm^2)**	**Double Blind: Rivastigmine (15 cm^2)**	**Extended Open Label (10 cm^2)**
Number of Participants Analyzed [units: participants]	**1582**	**283**	**280**	**457**
Number of Patients With Adverse Events, Serious Adverse Events and Discontinuations Due to Adverse Events [units: Participants]	**1135**	**193**	**210**	**263**

No statistical analysis provided for Number of Patients With Adverse Events, Serious Adverse Events and Discontinuations Due to Adverse Events

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	30 days after a maximum of 96 weeks treatment
Additional Description	The safety set included all patients who received at least one dose of study medication and who had at least one post-baseline safety assessment.

Reporting Groups

	Description
Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	Safety population Initial Open Label (Safety-IOL) - This population consisted of all patients who received at least 1 dose of study drug during the initial open label phase and had at least 1 post baseline safety assessment during the same phase.
Double Blind: Rivastigmine (10 cm^2)	Safety population Double Blind (Safety-DB) - This population included all patients who were randomized, received at least 1 dose of study drug during the double blind phase and had at least 1 post-randomization safety assessment during the double blind phase. Patients were analyzed according to treatment received.
Double Blind: Rivastigmine (15 cm^2)	Safety population Double Blind (Safety-DB) - This population included all patients who were randomized, received at least 1 dose of study drug during the double blind phase and had at least 1 post-randomization safety assessment during the double blind phase. Patients were analyzed according to treatment received.
Extended Open Label: Rivastigmine (10 cm^2)	Safety population Extended Open Label (Safety-EOL) - This population consisted of all patients who received at least 1 dose of study drug during the extended open label phase and had at least 1 post baseline safety assessment during the same phase.

Serious Adverse Events

	Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	**Double Blind: Rivastigmine (10 cm^2)**	**Double Blind: Rivastigmine (15 cm^2)**	**Extended Open Label: Rivastigmine (10 cm^2)**
Total, serious adverse events				
# participants affected / at risk	**227/1582 (14.35%)**	**44/283 (15.55%)**	**44/280 (15.71%)**	**59/457 (12.91%)**
Blood and lymphatic system disorders				
Anaemia †1				

# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Coagulopathy †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Haemorrhagic anaemia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Lymphadenopathy †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Cardiac disorders				
Acute coronary syndrome †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Acute myocardial infarction †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Angina pectoris †1				
# participants affected / at risk	2/1582 (0.13%)	2/283 (0.71%)	0/280 (0.00%)	1/457 (0.22%)
Aortic valve calcification †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Arrhythmia †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Atrial fibrillation †1				
# participants affected / at risk	9/1582 (0.57%)	2/283 (0.71%)	0/280 (0.00%)	3/457 (0.66%)
Atrial thrombosis †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Atrioventricular block complete †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Bradyarrhythmia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Bradycardia †1				
# participants affected / at risk	3/1582 (0.19%)	1/283 (0.35%)	2/280 (0.71%)	0/457 (0.00%)
Bundle branch block left †1				

# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Cardiac arrest †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Cardiac failure †1				
# participants affected / at risk	8/1582 (0.51%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Cardiac failure congestive †1				
# participants affected / at risk	2/1582 (0.13%)	1/283 (0.35%)	0/280 (0.00%)	1/457 (0.22%)
Cardio-respiratory arrest †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Cardiomyopathy †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Coronary artery disease †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Coronary artery stenosis †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Left ventricular failure †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Myocardial infarction †1				
# participants affected / at risk	6/1582 (0.38%)	2/283 (0.71%)	0/280 (0.00%)	0/457 (0.00%)
Myocardial ischaemia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Sick sinus syndrome †1				
# participants affected / at risk	1/1582 (0.06%)	2/283 (0.71%)	1/280 (0.36%)	1/457 (0.22%)
Sinus bradycardia †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Tachyarrhythmia †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Tachycardia †1				

# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	1/280 (0.36%)	0/457 (0.00%)
Tachycardia paroxysmal [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Ear and labyrinth disorders				
Vertigo [†1]				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Endocrine disorders				
Adrenal insufficiency [†1]				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Hyperthyroidism [†1]				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Thyroid disorder [†1]				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Eye disorders				
Cataract [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Visual acuity reduced [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Gastrointestinal disorders				
Abdominal discomfort [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Abdominal pain [†1]				
# participants affected / at risk	5/1582 (0.32%)	0/283 (0.00%)	2/280 (0.71%)	0/457 (0.00%)
Abdominal pain upper [†1]				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	1/457 (0.22%)
Colitis [†1]				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Colonic polyp [†1]				

# participants affected / at risk	**1/1582 (0.06%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Diarrhoea †1				
# participants affected / at risk	**5/1582 (0.32%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Duodenal ulcer haemorrhage †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Gastric ulcer haemorrhage †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Gastritis †1				
# participants affected / at risk	**4/1582 (0.25%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Gastrointestinal disorder †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Gastrointestinal inflammation †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Gastrooesophageal reflux disease †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**0/457 (0.00%)**
Hernial eventration †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Hiatus hernia †1				
# participants affected / at risk	**2/1582 (0.13%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**0/457 (0.00%)**
Inguinal hernia †1				
# participants affected / at risk	**1/1582 (0.06%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Intestinal mass †1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Intestinal obstruction †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**2/457 (0.44%)**
Irritable bowel syndrome †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Nausea †1				

# participants affected / at risk	7/1582 (0.44%)	1/283 (0.35%)	1/280 (0.36%)	1/457 (0.22%)
Pancreatitis †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Pancreatitis acute †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Rectal haemorrhage †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	1/457 (0.22%)
Reflux oesophagitis †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Sigmoiditis †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Small intestinal obstruction †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Vomiting †1				
# participants affected / at risk	12/1582 (0.76%)	2/283 (0.71%)	3/280 (1.07%)	1/457 (0.22%)
General disorders				
Abasia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Asthenia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	2/457 (0.44%)
Catheter site haemorrhage †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Complication of device removal †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Device malfunction †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Fatigue †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)

Gait disturbance [†1]				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
General physical health deterioration [†1]				
# participants affected / at risk	**1/1582 (0.06%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Malaise [†1]				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Non-cardiac chest pain [†1]				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**0/457 (0.00%)**
Oedema peripheral [†1]				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**0/457 (0.00%)**
Pyrexia [†1]				
# participants affected / at risk	**1/1582 (0.06%)**	**1/283 (0.35%)**	**1/280 (0.36%)**	**0/457 (0.00%)**
Hepatobiliary disorders				
Cholecystitis [†1]				
# participants affected / at risk	**2/1582 (0.13%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Cholecystitis acute [†1]				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Cholelithiasis [†1]				
# participants affected / at risk	**2/1582 (0.13%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**2/457 (0.44%)**
Cryptogenic cirrhosis [†1]				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Infections and infestations				
Abdominal sepsis [†1]				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Bacteraemia [†1]				
# participants affected / at risk	**0/1582 (0.00%)**	**2/283 (0.71%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Catheter site infection [†1]				

# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Cellulitis †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Cholecystitis infective †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Cystitis †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Diverticulitis †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Febrile infection †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Gastritis viral †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Gastroenteritis †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Gastroenteritis viral †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Herpes zoster †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Infected skin ulcer †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Infection †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Lobar pneumonia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Meningitis †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Osteomyelitis †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)

Pneumonia †1				
# participants affected / at risk	**7/1582 (0.44%)**	**2/283 (0.71%)**	**4/280 (1.43%)**	**2/457 (0.44%)**
Pyelonephritis †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Renal abscess †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Respiratory tract infection †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Sepsis †1				
# participants affected / at risk	**2/1582 (0.13%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Sinusitis †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**0/457 (0.00%)**
Urinary tract infection †1				
# participants affected / at risk	**7/1582 (0.44%)**	**4/283 (1.41%)**	**4/280 (1.43%)**	**2/457 (0.44%)**
Urosepsis †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**2/280 (0.71%)**	**0/457 (0.00%)**
Viral infection †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Injury, poisoning and procedural complications				
Accidental overdose †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Anastomotic leak †1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Cerebral haemorrhage traumatic †1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Chest injury †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Concussion †1				

# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Facial bones fracture †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Fall †1				
# participants affected / at risk	12/1582 (0.76%)	1/283 (0.35%)	3/280 (1.07%)	0/457 (0.00%)
Femoral neck fracture †1				
# participants affected / at risk	4/1582 (0.25%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Femur fracture †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	1/280 (0.36%)	2/457 (0.44%)
Foot fracture †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Forearm fracture †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Fractured sacrum †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Head injury †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Hip fracture †1				
# participants affected / at risk	7/1582 (0.44%)	2/283 (0.71%)	0/280 (0.00%)	1/457 (0.22%)
Humerus fracture †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Injury †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Joint dislocation †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	2/457 (0.44%)
Joint sprain †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Ligament rupture †1				

# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Lower limb fracture [†1]				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Mental status changes postoperative [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Multiple injuries [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Patella fracture [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Pelvic fracture [†1]				
# participants affected / at risk	1/1582 (0.06%)	3/283 (1.06%)	0/280 (0.00%)	0/457 (0.00%)
Radius fracture [†1]				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	1/457 (0.22%)
Rib fracture [†1]				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Soft tissue injury [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Spinal compression fracture [†1]				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Spinal fracture [†1]				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Subdural haematoma [†1]				
# participants affected / at risk	2/1582 (0.13%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Thoracic vertebral fracture [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Tibia fracture [†1]				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Traumatic brain injury [†1]				

# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Traumatic fracture † 1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Traumatic haematoma † 1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Upper limb fracture † 1				
# participants affected / at risk	4/1582 (0.25%)	0/283 (0.00%)	1/280 (0.36%)	1/457 (0.22%)
Investigations				
Cardiac enzymes increased † 1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Heart rate increased † 1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
International normalised ratio increased † 1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Prostatic specific antigen increased † 1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Metabolism and nutrition disorders				
Decreased appetite † 1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	2/280 (0.71%)	1/457 (0.22%)
Dehydration † 1				
# participants affected / at risk	5/1582 (0.32%)	3/283 (1.06%)	3/280 (1.07%)	1/457 (0.22%)
Diabetes mellitus † 1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Failure to thrive † 1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	1/457 (0.22%)
Hyperglycaemia † 1				

# participants affected / at risk	1/1582 (0.06%)	2/283 (0.71%)	0/280 (0.00%)	0/457 (0.00%)
Hyperkalaemia †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Hypoglycaemia †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Hypokalaemia †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Hyponatraemia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Malnutrition †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Musculoskeletal and connective tissue disorders				
Bursitis †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Groin pain †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Intervertebral disc protrusion †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Muscle spasms †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Muscular weakness †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Musculoskeletal chest pain †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Neck pain †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Osteoarthritis †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)

Osteoporotic fracture †1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Pain in extremity †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**2/457 (0.44%)**
Periarthritis †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Spinal osteoarthritis †1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Synovial cyst †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Acute myeloid leukaemia †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Angiomyolipoma †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
B-cell lymphoma †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Basal cell carcinoma †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Benign breast neoplasm †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Bladder cancer †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Bladder neoplasm †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Breast cancer †1				
# participants affected / at risk	**2/1582 (0.13%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**

Breast cancer metastatic †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Bronchial carcinoma †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Cholesteatoma †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Colon cancer †1				
# participants affected / at risk	**0/1582 (0.00%)**	**2/283 (0.71%)**	**0/280 (0.00%)**	**2/457 (0.44%)**
Colon neoplasm †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Colorectal cancer †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Gastric cancer †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Hepatic neoplasm malignant †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**0/457 (0.00%)**
Leiomyosarcoma †1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Lip and/or oral cavity cancer †1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Lung adenocarcinoma †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Lung neoplasm †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Lung neoplasm malignant †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Lymphoma †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Malignant melanoma †1				

# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Malignant melanoma in situ †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Metastases to liver †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Metastases to lung †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Metastases to meninges †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Metastatic neoplasm †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Oesophageal carcinoma †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Prostate cancer †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Skin cancer †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Squamous cell carcinoma of skin †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Thyroid cancer †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Nervous system disorders				
Balance disorder †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Brain oedema †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Cerebellar haemorrhage †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Cerebral haemorrhage †1				

# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	1/280 (0.36%)	1/457 (0.22%)
Cerebral ischaemia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Cerebrovascular accident †1				
# participants affected / at risk	5/1582 (0.32%)	1/283 (0.35%)	2/280 (0.71%)	0/457 (0.00%)
Cognitive disorder †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Coma †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Convulsion †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Crying †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Dementia †1				
# participants affected / at risk	3/1582 (0.19%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Dementia Alzheimer's type †1				
# participants affected / at risk	3/1582 (0.19%)	2/283 (0.71%)	0/280 (0.00%)	1/457 (0.22%)
Dizziness †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	2/280 (0.71%)	1/457 (0.22%)
Dizziness postural †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Embolic cerebral infarction †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Encephalopathy †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Epilepsy †1				
# participants affected / at risk	2/1582 (0.13%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Extrapyramidal disorder †1				

# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Lethargy †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Loss of consciousness †1				
# participants affected / at risk	2/1582 (0.13%)	1/283 (0.35%)	2/280 (0.71%)	0/457 (0.00%)
Mental impairment †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Multiple system atrophy †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Neuroleptic malignant syndrome †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	1/280 (0.36%)	0/457 (0.00%)
Neurological decompensation †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Paraesthesia †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Presyncope †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	2/280 (0.71%)	1/457 (0.22%)
Psychomotor hyperactivity †1				
# participants affected / at risk	3/1582 (0.19%)	1/283 (0.35%)	1/280 (0.36%)	2/457 (0.44%)
Sciatica †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Senile dementia †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Status epilepticus †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Syncope †1				
# participants affected / at risk	14/1582 (0.88%)	3/283 (1.06%)	2/280 (0.71%)	3/457 (0.66%)
Transient ischaemic attack †1				
# participants affected / at risk	3/1582 (0.19%)	1/283 (0.35%)	0/280 (0.00%)	1/457 (0.22%)

VIIth nerve paralysis †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Psychiatric disorders				
Abnormal behaviour †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**1/457 (0.22%)**
Aggression †1				
# participants affected / at risk	**5/1582 (0.32%)**	**2/283 (0.71%)**	**2/280 (0.71%)**	**0/457 (0.00%)**
Agitation †1				
# participants affected / at risk	**6/1582 (0.38%)**	**2/283 (0.71%)**	**3/280 (1.07%)**	**0/457 (0.00%)**
Anxiety †1				
# participants affected / at risk	**2/1582 (0.13%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Confusional state †1				
# participants affected / at risk	**3/1582 (0.19%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**1/457 (0.22%)**
Delirium †1				
# participants affected / at risk	**4/1582 (0.25%)**	**2/283 (0.71%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Delusion †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Depressed mood †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Depression †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Disorientation †1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Fear †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Hallucination †1				
# participants affected / at risk	**2/1582 (0.13%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Hallucination, visual †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**

Insomnia †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Mental status changes †1				
# participants affected / at risk	**4/1582 (0.25%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**3/457 (0.66%)**
Panic attack †1				
# participants affected / at risk	**0/1582 (0.00%)**	**0/283 (0.00%)**	**1/280 (0.36%)**	**0/457 (0.00%)**
Paranoia †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Psychotic disorder †1				
# participants affected / at risk	**2/1582 (0.13%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Restlessness †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Suicidal ideation †1				
# participants affected / at risk	**0/1582 (0.00%)**	**2/283 (0.71%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Suicide attempt †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Renal and urinary disorders				
Dysuria †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Haematuria †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Nephrolithiasis †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**1/457 (0.22%)**
Obstructive uropathy †1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Renal failure †1				
# participants affected / at risk	**2/1582 (0.13%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Renal failure acute †1				

# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	1/280 (0.36%)	2/457 (0.44%)
Renal infarct †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Urinary incontinence †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Urinary retention †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Reproductive system and breast disorders				
Prostatitis †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Respiratory, thoracic and mediastinal disorders				
Acute respiratory distress syndrome †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Asthma †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Dyspnoea †1				
# participants affected / at risk	5/1582 (0.32%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Dyspnoea exertional †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Foreign body aspiration †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Haemothorax †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Pleurisy †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Pleuritic pain †1				

# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Pneumonia aspiration †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	1/280 (0.36%)	1/457 (0.22%)
Pneumonitis †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Pulmonary embolism †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	2/457 (0.44%)
Respiratory distress †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Respiratory failure †1				
# participants affected / at risk	2/1582 (0.13%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Wheezing †1				
# participants affected / at risk	0/1582 (0.00%)	0/283 (0.00%)	0/280 (0.00%)	1/457 (0.22%)
Skin and subcutaneous tissue disorders				
Decubitus ulcer †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Hyperhidrosis †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Psoriasis †1				
# participants affected / at risk	0/1582 (0.00%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Skin ulcer †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Vascular disorders				
Aortic aneurysm rupture †1				
# participants affected / at risk	1/1582 (0.06%)	0/283 (0.00%)	0/280 (0.00%)	0/457 (0.00%)
Deep vein thrombosis †1				
# participants affected / at risk	1/1582 (0.06%)	1/283 (0.35%)	0/280 (0.00%)	0/457 (0.00%)
Hypertension †1				

# participants affected / at risk	**2/1582 (0.13%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Hypertensive crisis † 1				
# participants affected / at risk	**1/1582 (0.06%)**	**0/283 (0.00%)**	**0/280 (0.00%)**	**0/457 (0.00%)**
Hypotension † 1				
# participants affected / at risk	**3/1582 (0.19%)**	**1/283 (0.35%)**	**2/280 (0.71%)**	**1/457 (0.22%)**
Peripheral arterial occlusive disease † 1				
# participants affected / at risk	**0/1582 (0.00%)**	**1/283 (0.35%)**	**0/280 (0.00%)**	**0/457 (0.00%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 13.1

Other Adverse Events

Hide Other Adverse Events

Time Frame	30 days after a maximum of 96 weeks treatment
Additional Description	The safety set included all patients who received at least one dose of study medication and who had at least one post-baseline safety assessment.

Frequency Threshold

Threshold above which other adverse events are reported	3%

Reporting Groups

	Description
Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	Safety population Initial Open Label (Safety-IOL) - This population consisted of all patients who received at least 1 dose of study drug during the initial open label phase and had at least 1 post baseline safety assessment during the same phase.
Double Blind: Rivastigmine (10 cm^2)	Safety population Double Blind (Safety-DB) - This population included all patients who were randomized, received at least 1 dose of study drug during the double blind phase and had at least 1 post-randomization safety assessment during the double blind phase. Patients were analyzed according to treatment received.

Double Blind: Rivastigmine (15 cm^2)	Safety population Double Blind (Safety-DB) - This population included all patients who were randomized, received at least 1 dose of study drug during the double blind phase and had at least 1 post-randomization safety assessment during the double blind phase. Patients were analyzed according to treatment received.
Extended Open Label: Rivastigmine (10 cm^2)	Safety population Extended Open Label (Safety-EOL) - This population consisted of all patients who received at least 1 dose of study drug during the extended open label phase and had at least 1 post baseline safety assessment during the same phase.

Other Adverse Events

	Initial Open Label: Rivastigmine (5 cm^2 / 10 cm^2)	Double Blind: Rivastigmine (10 cm^2)	Double Blind: Rivastigmine (15 cm^2)	Extended Open Label: Rivastigmine (10 cm^2)
Total, other (not including serious) adverse events				
# participants affected / at risk	**732/1582 (46.27%)**	**110/283 (38.87%)**	**151/280 (53.93%)**	**112/457 (24.51%)**
Gastrointestinal disorders				
Abdominal pain upper †1				
# participants affected / at risk	**17/1582 (1.07%)**	**3/283 (1.06%)**	**9/280 (3.21%)**	**4/457 (0.88%)**
Diarrhoea †1				
# participants affected / at risk	**73/1582 (4.61%)**	**13/283 (4.59%)**	**18/280 (6.43%)**	**4/457 (0.88%)**
Nausea †1				
# participants affected / at risk	**90/1582 (5.69%)**	**13/283 (4.59%)**	**33/280 (11.79%)**	**11/457 (2.41%)**
Vomiting †1				
# participants affected / at risk	**68/1582 (4.30%)**	**12/283 (4.24%)**	**27/280 (9.64%)**	**1/457 (0.22%)**
General disorders				
Application site erythema †1				

# participants affected / at risk	184/1582 (11.63%)	16/283 (5.65%)	18/280 (6.43%)	10/457 (2.19%)
Application site pruritus [†1]				
# participants affected / at risk	139/1582 (8.79%)	11/283 (3.89%)	11/280 (3.93%)	5/457 (1.09%)
Application site rash [†1]				
# participants affected / at risk	56/1582 (3.54%)	5/283 (1.77%)	6/280 (2.14%)	2/457 (0.44%)
Infections and infestations				
Urinary tract infection [†1]				
# participants affected / at risk	45/1582 (2.84%)	8/283 (2.83%)	11/280 (3.93%)	11/457 (2.41%)
Injury, poisoning and procedural complications				
Fall [†1]				
# participants affected / at risk	53/1582 (3.35%)	16/283 (5.65%)	19/280 (6.79%)	24/457 (5.25%)
Investigations				
Weight decreased [†1]				
# participants affected / at risk	44/1582 (2.78%)	8/283 (2.83%)	19/280 (6.79%)	12/457 (2.63%)
Metabolism and nutrition disorders				
Decreased appetite [†1]				
# participants affected / at risk	36/1582 (2.28%)	7/283 (2.47%)	16/280 (5.71%)	5/457 (1.09%)
Nervous system disorders				
Dizziness [†1]				
# participants affected / at risk	37/1582 (2.34%)	2/283 (0.71%)	10/280 (3.57%)	8/457 (1.75%)
Headache [†1]				

# participants affected / at risk	**62/1582 (3.92%)**	**11/283 (3.89%)**	**11/280 (3.93%)**	**7/457 (1.53%)**
Psychiatric disorders				
Agitation †1				
# participants affected / at risk	**42/1582 (2.65%)**	**14/283 (4.95%)**	**12/280 (4.29%)**	**5/457 (1.09%)**
Anxiety †1				
# participants affected / at risk	**56/1582 (3.54%)**	**7/283 (2.47%)**	**10/280 (3.57%)**	**10/457 (2.19%)**
Depression †1				
# participants affected / at risk	**65/1582 (4.11%)**	**13/283 (4.59%)**	**14/280 (5.00%)**	**15/457 (3.28%)**
Insomnia †1				
# participants affected / at risk	**40/1582 (2.53%)**	**7/283 (2.47%)**	**11/280 (3.93%)**	**6/457 (1.31%)**
Renal and urinary disorders				
Urinary incontinence †1				
# participants affected / at risk	**25/1582 (1.58%)**	**5/283 (1.77%)**	**9/280 (3.21%)**	**6/457 (1.31%)**
Vascular disorders				
Hypertension †1				
# participants affected / at risk	**53/1582 (3.35%)**	**8/283 (2.83%)**	**9/280 (3.21%)**	**8/457 (1.75%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 13.1

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:** The terms and conditions of Novartis' agreements with its investigators may vary. However, Novartis does not prohibit any investigator from publishing. Any publications from a single-site are postponed until the publication of the pooled data (i.e., data from all sites) in the clinical trial or disclosure of trial results in their entirety.

Results Point of Contact:

Name/Title: Study Director
Organization: Novartis
phone: 862 778 8300

No publications provided by Novartis

Publications automatically indexed to this study:

Grossberg G, Cummings J, Frölich L, Bellelli G, Molinuevo JL, Krahnke T, Strohmaier C. Efficacy of higher dose 13.3 mg/24 h rivastigmine patch on instrumental activities of daily living in patients with mild-to-moderate Alzheimer's disease. Am J Alzheimers Dis Other Demen. 2013 Sep;28(6):583-91. doi: 10.1177/1533317513495104.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
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Last Updated:	September 17, 2012
Health Authority:	United Kingdom: Medicines and Healthcare Products Regulatory Agency Germany: Federal Institute for Drugs and Medical Devices France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Italy: Agenzia Italiana del Farmaco (AIFA) Spain: Agencia Española del Medicamento y Productos Sanitarios (AEMPS) Canada: Therapeutic Products Directorate (TPD) Switzerland: Swissmedic United States: Food and Drug Administration