ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 09/22/2011

ClinicalTrials.gov ID: NCT00649220

Study Identification

Unique Protocol ID:	MRZ 90001-0716/1
Brief Title:	Memantine and Antipsychotics Use (MemAP)
Official Title:	Prospective, Single-arm, Multi-centre, Open-label Study to Investigate the Potential to Reduce Concomitant Antipsychotics Use in Patients With Moderate to Severe Dementia of Alzheimer's Type (DAT) Treated With Memantine
Secondary IDs:	2007-004489-41 [EudraCT Number]

Study Status

Record Verification:	September 2011
Overall Status:	Terminated [Study terminated due to too slow enrollment]
Study Start:	July 2008
Primary Completion:	May 2009 [Actual]
Study Completion:	June 2009 [Actual]

Sponsor/Collaborators

Sponsor:	Merz Pharmaceuticals GmbH
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: 2007351 Board Name: Ethics Committee of the Doctor's Association North-Rhine Board Affiliation: Working Group Medical Ethics Committees in Germany Phone: Email: ethik@aekno.de
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Germany: Federal Institute for Drugs and Medical Devices

Study Description

Brief Summary:	To investigate the potential to reduce concomitant antipsychotic medication use in subjects with moderate dementia of Alzheimer's type, treated with memantine.
Detailed Description:	

Conditions

Conditions:	Alzheimer's Disease
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	N/A
Endpoint Classification:	Efficacy Study
Enrollment:	19 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Memantine	Drug: Memantine memantine tablets, twice a day (bid), for 20 weeks

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 50 Years

Maximum Age: 85 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion criteria:

- Current diagnosis of probable Alzheimer's disease consistent with NINCDS-ADRDA criteria or with DSM IV TR criteria for Dementia of the Alzheimer’s type.
- MRI or CT scan supporting the diagnosis of DAT without indications of any relevant other CNS disorders.
- Patients treated with any acetylcholinesterase inhibitor (AChEI) man be included.
- The patient should have German as a mother-tongue or at least speak the language fluently.

Exclusion criteria:

- Evidence (including CT/MRI results) of any clinically significant central nervous system disease other than Alzheimer’s disease.
- Modified Hachinski Ischemia score greater than 4 at screening.
- Intake of any medication that is contra-indicated in combination with memantine.
- Treatment with depot antipsychotics.
- History of severe drug allergy, or hypersensitivity, or patients with known hypersensitivity to memantine, amantadine or lactose.
- Known or suspected history of alcoholism or drug abuse within the past 10 years.
- Previous treatment with memantine or participation in an investigational study with memantine.

Contacts/Locations

Study Officials: Medical Expert
Study Director

Merz Pharmaceuticals GmbH

Locations: Germany
Alexianer Hospital
Krefeld, North-Rhine-Westphalia, Germany

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Overall Study

	Memantine
Started	19
Completed	16
Not Completed	3
Adverse Event	2
Withdrawal by Subject	1

Baseline Characteristics

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Baseline Measures

	Memantine
Number of Participants	19
Age, Continuous [units: years] Mean (Standard Deviation)	72.4 (9.7)
Age, Customized Between 50 and 85 years [units: participants]	19
Gender, Male/Female [units: participants]	
Female	10
Male	9
Region of Enrollment Germany [units: participants]	19

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Maximum Dose Reduction of Antipsychotics (AP) in Percent of Defined Daily Dose (DDD) From Baseline to a Post-baseline Visit at Which the Value of the Visual Analogue Scale (VAS) Compared With the Baseline Value Was =< 15 Percent.
Measure Description	VAS: see #8. Mean “percent of the total Defined Daily Dose (DDD)”, averaged over one week, was calculated. Total DDD was calculated as sum of DDD for each AP drug. DDD is the assumed average maintenance dose per day defined by WHO. The reduction of AP Δ [percent] was calculated as a difference between the mean total DDD recorded at baseline and the mean total DDD recorded at the respective week. Measurements from those post-baseline visits were taken into account only when the value of the VAS was not substantially worse compared to baseline.
Time Frame	Week 8-20 post baseline
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT)

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Measured Values

	Memantine
Number of Participants Analyzed	19
Maximum Dose Reduction of Antipsychotics (AP) in Percent of Defined Daily Dose (DDD) From Baseline to a Post-baseline Visit at Which the Value of the Visual Analogue Scale (VAS) Compared With the Baseline Value Was =< 15 Percent. [units: Percent of daily dose [DDD]] Mean (Standard Deviation)	-13.9 (13.58)

Statistical Analysis 1 for Maximum Dose Reduction of Antipsychotics (AP) in Percent of Defined Daily Dose (DDD) From Baseline to a Post-baseline Visit at Which the Value of the Visual Analogue Scale (VAS) Compared With the Baseline Value Was =< 15 Percent.

Statistical Analysis Overview	Comparison Groups	Memantine
	Comments	Two-side, paired t-test on the null hypothesis that antipsychotics are reduced by 10% compared to baseline
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.22626
	Comments	[Not specified]
	Method	t-test, 2 sided
	Comments	[Not specified]

Statistical Analysis 2 for Maximum Dose Reduction of Antipsychotics (AP) in Percent of Defined Daily Dose (DDD) From Baseline to a Post-baseline Visit at Which the Value of the Visual Analogue Scale (VAS) Compared With the Baseline Value Was =< 15 Percent.

Statistical Analysis Overview	Comparison Groups	Memantine
	Comments	Wilcoxon signed rank test on the null hypothesis that antipsychotics are reduced by 10% compared to baseline
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.34192
	Comments	[Not specified]
	Method	Other [Wilcoxon signed rank test]
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Reduction of Antipsychotic Drug Dose From Baseline to Week 8, 12, 16 and/or 20.
Measure Description	See #1 and #8. Change of <0 reveals a reduction of AP compared to baseline.
Time Frame	Week 8-20 post Baseline
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Week 8: n=16; Week 12: n=14; Week 16: n=13; Week 20: n=15

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Measured Values

	Memantine
Number of Participants Analyzed	15
Reduction of Antipsychotic Drug Dose From Baseline to Week 8, 12, 16 and/or 20. [units: Percent of daily dose [DDD]] Mean (Standard Deviation)	
Week 8	-4.4 (5.53)
Week 12	-8.2 (12.38)
Week 16	-10.6 (13.49)
Week 20	-14.9 (15.05)

3. Secondary Outcome Measure:

Measure Title	Change in the Mini-Mental State Examination (MMSE) Score Value From Baseline to Week 20.
Measure Description	MMSE is a brief, physician–administered scale, designed for measuring the cognitive functions, such as: orientation, memory, attention, naming, and comprehension. The scoring range of MMSE is 0 to 30 points. A score of 23 or lower is indicative of cognitive impairment. Change of >0 reveals an improvement compared to baseline.
Time Frame	Week 20 post baseline
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT)

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Measured Values

	Memantine
Number of Participants Analyzed	15
Change in the Mini-Mental State Examination (MMSE) Score Value From Baseline to Week 20. [units: units on a scale] Mean (Standard Deviation)	0.9 (3.44)

4. Secondary Outcome Measure:

Measure Title	Change of "Test for the Early Detection of Dementia With Discrimination From Depression [TE4D]" Score Value From Baseline to Week 4, 8, 12, 16, and/or 20 - First Part: Total Dementia
Measure Description	TE4D is a psychometric, physician-administered test that is used for both screening subjects with early dementia and monitoring the clinical progress of the disease. The first part consists of 9 items, which assess different symptoms associated with dementia such as memory, time-orientation, etc. The scoring range is 0 to 50 points. A score of 35 or lower is an indication of dementia. A change >0 represents an improvement.
Time Frame	Week 4-20 post baseline
Safety Issue?	No

Analysis Population Description

Intent to treat (ITT).

Week 4: n=18; Week 8: n=17; Week 12: n=16; Week 16: n=16; Week 20: n=17

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Measured Values

	Memantine
Number of Participants Analyzed	17
Change of "Test for the Early Detection of Dementia With Discrimination From Depression [TE4D]" Score Value From Baseline to Week 4, 8, 12, 16, and/or 20 - First Part: Total Dementia [units: units on a scale] Mean (Standard Deviation)	
Week 4	-2.3 (7.64)
Week 8	-0.3 (5.31)
Week 12	-1.3 (4.48)
Week 16	0.7 (5.39)
Week 20	1.4 (4.2)

5. Secondary Outcome Measure:

Measure Title	Change of "Test for the Early Detection of Dementia With Discrimination From Depression [TE4D]" Score Value From Baseline to Week 4, 8, 12, 16, and/or 20 - Second Part: Total Depression
Measure Description	TE4D is a psychometric, physician-administered test that is used for both screening subjects with early dementia and monitoring the clinical progress of the disease. The second part consists of a proxy rating and a self-assessment rating. The scoring range of each rating is 1 to 10. The maximum total score of 10 corresponds to severe depression. A change <0 reveals an improvement compared to baseline.
Time Frame	Week 4-20 post Baseline
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Week 4: n=18; Week 8: n=17; Week 12: n=16; Week 16: n=16; Week 20: n=17

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Measured Values

	Memantine
Number of Participants Analyzed	17
Change of "Test for the Early Detection of Dementia With Discrimination From Depression [TE4D]" Score Value From Baseline to Week 4, 8, 12, 16, and/or 20 - Second Part: Total Depression [units: units on a scale] Mean (Standard Deviation)	
Week 4	2.5 (4.84)
Week 8	1.6 (3.97)
Week 12	-0.1 (3.26)
Week 16	-0.2 (2.07)
Week 20	-0.4 (2.09)

6. Secondary Outcome Measure:

Measure Title	Change of Modified Alzheimer's Disease Cooperative Study - Activities of Daily Living Inventory (ADCS-ADLB19) Score Value From Baseline to Week 4, 8, 12, 16, and/or 20.
Measure Description	The modified ADCS-ADL19 is comprehensive battery of ADL questions aimed to measure the functional ability of subjects with Dementia of Alzheimer’s type over a broad range of dementia severity. It has a scoring range of 0 to 54 with the lower scores indicating greater functional impairment. Each ADL item was rated from the highest level of independent performance to complete loss. Change of >0 reveals an improvement compared to baseline.
Time Frame	Week 4-20 post Baseline
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Week 4: n=18; Week 8: n=17; Week 12: n=16; Week 16: n=16; Week 20: n=18

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Measured Values

	Memantine
Number of Participants Analyzed	18
Change of Modified Alzheimer's Disease Cooperative Study - Activities of Daily Living Inventory (ADCS-ADLB19) Score Value From Baseline to Week 4, 8, 12, 16, and/or 20. [units: Units on a Scale] Mean (Standard Deviation)	
Week 4	-0.7 (6.33)
Week 8	2.2 (8.09)
Week 12	3.8 (11.07)
Week 16	3.8 (11.27)
Week 20	2.4 (11.08)

7. Secondary Outcome Measure:

Measure Title	Change of Nurses' Observation Scale for Geriatric Patients [NOSGER] Total Score Value From Baseline to Week 4, 8, 12, 16, and/or 20
Measure Description	NOSGER is a comprehensive scale, which contains 30 items of behavior, each rated on a 5-point scale according to the frequency of occurrence by direct observation. Item scores are summarized into 6 dimension scores: memory, instrumental activities of daily life, self-care, mood, social behavior, and disturbing behavior. The NOSGER has a scoring range of 30 to 150 with the higher scores indicating worse subject’s status. The items in each group are rated for their frequency ranging from 1 (never) to 5 (always). A change of <0 reveals an improvement compared to baseline.
Time Frame	Week 4-20 post Baseline

Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Week 4: n=18; Week 8: n=17; Week 12: n=16; Week 16: n=16; Week 20: n=17

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Measured Values

	Memantine
Number of Participants Analyzed	18
Change of Nurses' Observation Scale for Geriatric Patients [NOSGER] Total Score Value From Baseline to Week 4, 8, 12, 16, and/or 20 [units: Units on a scale] Mean (Standard Deviation)	
Week 4	-0.4 (10.9)
Week 8	-2.1 (10.31)
Week 12	-5.4 (13.29)
Week 16	-8.4 (18.74)
Week 20	-7.9 (19.02)

8. Secondary Outcome Measure:

Measure Title	Change in the VAS Score From Baseline to Week 8, 12, 16 and/or 20.
Measure Description	VAS is a report device to measure the subject’s burden caused by behavioral symptoms. To measure the burden on the VAS only the first 3 items of the Neuropsychiatric Inventory (NPI) Questionnaire were considered (delusions, hallucinations (visual and auditory), and agitation / aggression). The VAS consists of a 100 mm horizontal line, anchored at the ends with the reference “not at all” and “extremely". The VAS score was determined by measuring in mm from the left hand end of the line to the point, where the investigator had marked the magnitude of a subject’s burden.
Time Frame	Week 8-20 post Baseline

Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Week 8: n=17; Week 12: n=16; Week 16: n=16; Week 20: n=18

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Measured Values

	Memantine
Number of Participants Analyzed	18
Change in the VAS Score From Baseline to Week 8, 12, 16 and/or 20. [units: Units on a scale [cm]] Mean (Standard Deviation)	
Week 8	-1.5 (1.94)
Week 12	-1.7 (2.53)
Week 16	-1.2 (2.86)
Week 20	-1.4 (2.46)

Reported Adverse Events

Time Frame	All SAEs/AEs from baseline until 4 weeks after end of treatment (in total 20 weeks)
Additional Description	The table of "Other Adverse Events" includes all non-serious AEs. The investigator asked the patient for AEs systematically at each visit.

Reporting Groups

	Description
Memantine	Memantine tablets, twice a day (bid).

Serious Adverse Events

	Memantine	
	Affected/At Risk (%)	# Events
Total	2/19 (10.53%)	
Psychiatric disorders		
Agitation [A] †	1/19 (5.26%)	1
Depression [A] †	1/19 (5.26%)	1
Sleep Disturbances [A] †	1/19 (5.26%)	1

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Memantine	
	Affected/At Risk (%)	# Events
Total	7/19 (36.84%)	
Gastrointestinal disorders		
Diarrhoea [A] †	1/19 (5.26%)	1
Epigastric discomfort [A] †	1/19 (5.26%)	1
Haemorrhoidal haemorrhage [A] †	1/19 (5.26%)	1
Nausea [A] †	1/19 (5.26%)	1
General disorders		
Fatigue [A] †	2/19 (10.53%)	2
Infections and infestations		
Nasopharyngitis [A] †	1/19 (5.26%)	1
Urinary tract infection [A] †	1/19 (5.26%)	1
Injury, poisoning and procedural complications		
Joint sprain [A] †	1/19 (5.26%)	1

	Memantine	
	Affected/At Risk (%)	# Events
Psychiatric disorders		
Agitation [A] †	1/19 (5.26%)	1
Anxiety [A] †	1/19 (5.26%)	1
Insomnia [A] †	1/19 (5.26%)	1
Listless [A] †	1/19 (5.26%)	1
Sleep-related eating disorder [A] †	1/19 (5.26%)	1

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 12

Limitations and Caveats

Early termination due to too slow enrollment lead to a small sample size, limiting the ability for confirmatory analysis. All analysis of the primary efficacy endpoint were treated as exploratory.

More Information

Certain Agreements:

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

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

No results to be published without written agreement by sponsor; manuscripts to be sent to sponsor at least 6 weeks before submission. Sponsor to give written opinion within 30 days. Sponsor is entitled to exert influence on the contents of publications, to postpone publications up to 36 months after end of the study, and to name co-authors. In case of justified doubts of sponsor, the INVESTIGATOR will consider these doubts in the publication as long as the scientific neutrality is not affected.

Results Point of Contact:

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