Twenty-six Week Extension Trial of Org 50081 (Esmirtazapine) in Outpatients With Chronic Primary Insomnia (176003/P05721/MK-8265-007)

This study has been terminated.

(This trial was stopped prematurely due to the Sponsor's decision not to continue the development of esmertazapine for this indication.)

Sponsor:
Merck Sharp & Dohme Corp.

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00750919

First received: September 10, 2008
Last updated: July 2, 2015
Last verified: July 2015
History of Changes

Purpose

This trial is a 26-week, open label extension trial to investigate safety and explore efficacy of esmertazapine in participants with insomnia who completed protocol 21106/P05701/MK-8265-002 (NCT00631657).

Condition	Intervention	Phase
Sleep Initiation and Maintenance Disorders Mental Disorders Dyssomnias Sleep Disorders Sleep Disorders, Intrinsic	Drug: esmirtazapine	Phase 3

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Twenty-six Weeks, Open-label Extension Trial to Evaluate Safety and Efficacy of Org 50081 (Esmirtazapine) in Outpatients With Chronic Primary Insomnia Who Completed Clinical Trial Protocol 21106

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Change From Baseline in Total Sleep Time (TST) [Time Frame: Baseline and Week 26] [Designated as safety issue: No]

  TST was defined as the time recorded for sleep diary question 6 "how much time did you actually spend sleeping" as reported by the participants using a LogPad (hand-held electronic data capture device). Baseline was defined as the TST from the last week of the base study.

Daily diary data were converted to weekly averages. For each treatment week the non-missing diary data of that week were taken into account; if a treatment week had three non-missing morning diaries or less, the data of the previous week were taken into account, weighing the data of both weeks, using the number of observed diaries as weights (weighted mean); if no diary data were available for a treatment week the data were considered as missing and were not imputed.

- Number of Participants Experiencing Adverse Events (AEs) [Time Frame: Up to 30 weeks] [Designated as safety issue: Yes]

  An adverse event is any unfavorable and unintended change in the structure, function, or chemistry of the body whether or not considered related to the study treatment.

- Number of Participants Discontinuing Due to AEs [Time Frame: Up to 26 weeks] [Designated as safety issue: Yes]

  An adverse event is any unfavorable and unintended change in the structure, function, or chemistry of the body whether or not considered related to the study treatment.

Secondary Outcome Measures:

- Change From Baseline in Sleep Latency (SL) [Time Frame: Baseline and Week 26] [Designated as safety issue: No]

  SL was defined as the time recorded for sleep diary question 3 "how long did it take you to fall asleep', " as reported by the participants using a LogPad (hand-held electronic data capture device). Baseline was defined as the SL from the last week of the base study. Daily diary data were converted to weekly averages. For each treatment week the non-missing diary data of that week were taken into account; if a treatment week had three non-missing morning diaries or less, the data of the previous week were taken into account, weighing the data of both weeks, using the number of observed diaries as weights (weighted mean); if no diary data were available for a treatment week the data were considered as missing and were not imputed.

- Change From Baseline in Wake Time After Sleep Onset (WASO) [Time Frame: Baseline and Week 26] [Designated as safety issue: No]

  WASO was defined as the time recorded for sleep diary question 5 "how much time were you awake, after falling asleep initially" as reported by the participants using a LogPad (hand-held electronic data capture device). Baseline was defined as the WASO from the last week of the base study. Daily diary data were converted to weekly averages. For each treatment week the non-missing diary data of that week were taken into account; if a treatment week had three non-missing morning diaries or less, the data of the previous week were taken into account, weighing the data of both weeks, using the number of observed diaries as weights (weighted mean); if no diary data were available for a treatment week the data were considered as missing and were not imputed.

Enrollment:	184
Study Start Date:	October 2008
Study Completion Date:	March 2010
Primary Completion Date:	March 2010 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Esmirtazapine Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months.	Drug: esmirtazapine

Eligibility

Ages Eligible for Study:	18 Years to 65 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- Sign written informed consent
- Completed clinical trial 21106/P05701/MK-8265-002

Exclusion Criteria:

- Any (serious) adverse event, medical condition or required concomitant medication deemed relevant for exclusion in trial 21106/P05071/MK-8265-002 as judged by the investigator

- Were significantly non compliant with protocol criteria and procedures of trial 21106/P05701/MK-8265-002, as judged by the investigator
- Pregnancy

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.

No Contacts or Locations Provided

More Information

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00750919 History of Changes
Other Study ID Numbers:	P05721 176003 2007-005237-10
Study First Received:	September 10, 2008
Results First Received:	May 22, 2014
Last Updated:	July 2, 2015
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Disease	Dyssomnias
Mental Disorders	Nervous System Diseases
Parasomnias	Neurologic Manifestations
Psychotic Disorders	Pathologic Processes
Sleep Disorders	Schizophrenia and Disorders with Psychotic Features
Sleep Disorders, Intrinsic	Signs and Symptoms
Sleep Initiation and Maintenance Disorders	

ClinicalTrials.gov processed this record on May 08, 2016

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First received: September 10, 2008
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History of Changes

Results First Received: May 22, 2014

Study Type:	Interventional
Study Design:	Endpoint Classification: Safety/Efficacy Study; Intervention Model: Single Group Assignment; Masking: Open Label; Primary Purpose: Treatment
Conditions:	Sleep Initiation and Maintenance Disorders Mental Disorders Dyssomnias Sleep Disorders Sleep Disorders, Intrinsic
Intervention:	Drug: esmirtazapine

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
Participants who completed P05701 (Base study NCT00631657) were eligible to enroll on P05721 (Extension study).

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
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Participant Flow: Overall Study

	Esmirtazapine
STARTED	**184**
COMPLETED	**126**
NOT COMPLETED	**58**
Adverse Event	**9**
Withdrawal by Subject	**1**
Lack of Efficacy	**8**
Could not cooperate, unrelated to trial	**4**
Unspecified	**36**

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
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Baseline Measures

	Esmirtazapine
Number of Participants [units: participants]	**184**
Age [units: years] Mean (Standard Deviation)	**47.8 (11.5)**
Gender [units: Participants]	
Female	**111**
Male	**73**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline in Total Sleep Time (TST) [Time Frame: Baseline and Week 26]

Measure Type	Primary
Measure Title	Change From Baseline in Total Sleep Time (TST)
Measure Description	TST was defined as the time recorded for sleep diary question 6 "how much time did you actually spend sleeping" as reported by the participants using a LogPad (hand-held electronic data capture device). Baseline was defined as the TST from the last week of the base study. Daily diary data were converted to weekly averages. For each treatment week the non-missing diary data of that week were taken into account; if a treatment week had three non-missing morning diaries or less, the data of the previous week were taken into account, weighing the data of both weeks, using the number of observed diaries as weights (weighted mean); if no diary data were available for a treatment week the data were considered as missing and were not imputed.
Time Frame	Baseline and Week 26
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.
The All-Subjects-Treated (AST) population consisted of all participants who received at least one dose of esmertazapine in the extension study.

Reporting Groups

	Description
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Measured Values

	Esmirtazapine
Number of Participants Analyzed [units: participants]	**184**
Change From Baseline in Total Sleep Time (TST) [units: Minutes per night] Mean (Standard Deviation)	
Baseline measure (n=184)	**368.1 (91.5)**
Change from baseline at Week 26 (n=123)	**9.7 (56.1)**

No statistical analysis provided for Change From Baseline in Total Sleep Time (TST)

2. Primary: Number of Participants Experiencing Adverse Events (AEs) [Time Frame: Up to 30 weeks]

Measure Type	Primary
Measure Title	Number of Participants Experiencing Adverse Events (AEs)

Measure Description	An adverse event is any unfavorable and unintended change in the structure, function, or chemistry of the body whether or not considered related to the study treatment.
Time Frame	Up to 30 weeks
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 AST population consisted of all participants who received at least one dose of esmertazapine in the extension study.

Reporting Groups

	Description
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Measured Values

	Esmirtazapine
Number of Participants Analyzed [units: participants]	**184**
Number of Participants Experiencing Adverse Events (AEs) [units: Participants]	**127**

No statistical analysis provided for Number of Participants Experiencing Adverse Events (AEs)

3. Primary: Number of Participants Discontinuing Due to AEs [Time Frame: Up to 26 weeks]

Measure Type	Primary
Measure Title	Number of Participants Discontinuing Due to AEs
Measure Description	An adverse event is any unfavorable and unintended change in the structure, function, or chemistry of the body whether or not considered related to the study treatment.
Time Frame	Up to 26 weeks
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 AST population consisted of all participants who received at least one dose of esmertazapine in the extension study.

Reporting Groups

	Description
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Measured Values

	Esmirtazapine
Number of Participants Analyzed [units: participants]	**184**
Number of Participants Discontinuing Due to AEs [units: Participants]	**9**

No statistical analysis provided for Number of Participants Discontinuing Due to AEs

4. Secondary: Change From Baseline in Sleep Latency (SL) [Time Frame: Baseline and Week 26]

Measure Type	Secondary
Measure Title	Change From Baseline in Sleep Latency (SL)
Measure Description	SL was defined as the time recorded for sleep diary question 3 "how long did it take you to fall asleep', " as reported by the participants using a LogPad (hand-held electronic data capture device). Baseline was defined as the SL from the last week of the base study. Daily diary data were converted to weekly averages. For each treatment week the non-missing diary data of that week were taken into account; if a treatment week had three non-missing morning diaries or less, the data of the previous week were taken into account, weighing the data of both weeks, using the number of observed diaries as weights (weighted mean); if no diary data were available for a treatment week the data were considered as missing and were not imputed.
Time Frame	Baseline and Week 26
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.
The All-Subjects-Treated (AST) population consisted of all participants who received at least one dose of esmertazapine in the extension study.

Reporting Groups

	Description
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Measured Values

	Esmirtazapine
Number of Participants Analyzed [units: participants]	**148**
Change From Baseline in Sleep Latency (SL) [units: Minutes per night] Mean (Standard Deviation)	
Baseline measure (n=184)	**38.7 (32.0)**
Change from baseline at Week 26 (n=123)	**-1.5 (39.1)**

No statistical analysis provided for Change From Baseline in Sleep Latency (SL)

5. Secondary: Change From Baseline in Wake Time After Sleep Onset (WASO) [Time Frame: Baseline and Week 26]

Measure Type	Secondary
Measure Title	Change From Baseline in Wake Time After Sleep Onset (WASO)
Measure Description	WASO was defined as the time recorded for sleep diary question 5 "how much time were you awake, after falling asleep initially" as reported by the participants using a LogPad (hand-held electronic data capture device). Baseline was defined as the WASO from the last week of the base study. Daily diary data were converted to weekly averages. For each treatment week the non-missing diary data of that week were taken into account; if a treatment week had three non-missing morning diaries or less, the data of the previous week were taken into account, weighing the data of both weeks, using the number of observed diaries as weights (weighted mean); if no diary data were available for a treatment week the data were considered as missing and were not imputed.
Time Frame	Baseline and Week 26
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.
The AST population consisted of all participants who received at least one dose of esmertazapine in the extension study.

Reporting Groups

	Description
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Measured Values

	Esmirtazapine
Number of Participants Analyzed [units: participants]	**148**
Change From Baseline in Wake Time After Sleep Onset (WASO) [units: Minutes per night] Mean (Standard Deviation)	
Baseline measure (n=184)	**40.0 (43.5)**
Change from baseline at Week 26 (n=123)	**-5.4 (32.3)**

No statistical analysis provided for Change From Baseline in Wake Time After Sleep Onset (WASO)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Nonserious AEs were collected from first dispensing of study drug up to 7 days after last dose of study drug. Serious AEs were collected from first dispensing of study drug up to 30 days after last dose of study drug.

Additional Description	No text entered.

Reporting Groups

	Description
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Serious Adverse Events

	Esmirtazapine
Total, serious adverse events	
# participants affected / at risk	**3/184 (1.63%)**
Cardiac disorders	
Acute myocardial infarction † 1	
# participants affected / at risk	**1/184 (0.54%)**
# events	**1**
Musculoskeletal and connective tissue disorders	
Intervertebral disc degeneration † 1	
# participants affected / at risk	**1/184 (0.54%)**
# events	**1**
Surgical and medical procedures	
Strabismus correction † 1	
# participants affected / at risk	**1/184 (0.54%)**
# events	**1**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 13.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Nonserious AEs were collected from first dispensing of study drug up to 7 days after last dose of study drug. Serious AEs were collected from first dispensing of study drug up to 30 days after last dose of study drug.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Esmirtazapine	Participants receive esmirtazapine 4.5 mg tablet, orally, once daily (QD) for up to 6 months

Other Adverse Events

	Esmirtazapine
Total, other (not including serious) adverse events	
# participants affected / at risk	**59/184 (32.07%)**
Infections and infestations	
Nasopharyngitis † 1	
# participants affected / at risk	**19/184 (10.33%)**
# events	**20**
Investigations	
Weight increased † 1	
# participants affected / at risk	**11/184 (5.98%)**
# events	**12**
Nervous system disorders	
Headache † 1	
# participants affected / at risk	**10/184 (5.43%)**
# events	**13**
Somnolence † 1	
# participants affected / at risk	**10/184 (5.43%)**
# events	**11**
Psychiatric disorders	
Insomnia † 1	
# participants affected / at risk	**23/184 (12.50%)**
# events	**23**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 13.0

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

This study was terminated due to the Sponsor's decision not to continue development of esmertazapine for this indication.

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.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp.
phone: 1-800-672-6372
e-mail: ClinicalTrialsDisclosure@merck.com

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00750919 History of Changes
Other Study ID Numbers:	P05721 176003 (Other Identifier: Organon Protocol Number) 2007-005237-10 (EudraCT Number)
Study First Received:	September 10, 2008
Results First Received:	May 22, 2014
Last Updated:	July 2, 2015
Health Authority:	United States: Food and Drug Administration

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