Almorexant (ACT 078573) in Adult Subjects With Chronic Primary Insomnia (RESTORA 1)

This study has been completed.

Sponsor:
Midnight Pharma, LLC

Information provided by (Responsible Party):
Midnight Pharma, LLC

ClinicalTrials.gov Identifier:
NCT00608985

First received: January 11, 2008
Last updated: February 11, 2016
Last verified: February 2016
History of Changes

Results First Received: December 21, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Treatment
Condition:	Primary Insomnia
Interventions:	Drug: almorexant Drug: Placebo Drug: zolpidem

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
First subject, first visit was on 28 April 2008. The last subject, last visit (safety follow-up) was on 30 September 2009.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
There was a screening period of 14 to 28 days. Two randomized subjects (one in each almorexant (ACT-078573) dose group) did not receive double-blind study treatment. The 'Started population' was defined as those participants who were randomized and treated.

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Participant Flow: Overall Study

	Placebo	Almorexant 100mg	Almorexant 200mg	Zolpidem 10mg
STARTED	177 [1]	186 [1]	176 [1]	168 [1]
Completed Double-blind Treatment	163	174	171	161
COMPLETED	161 [2]	173 [2]	170 [2]	159 [2]
NOT COMPLETED	16	13	6	9
Adverse Event	2	7	4	6
Administrative/Other	7	4	1	2
Withdrawal of Consent	5	1	1	1
Lost to Follow-up	2	1	0	0

[1] Randomized and started double-blind treatment

[2] Completed follow-up

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
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated
Total	Total of all reporting groups

Baseline Measures

	Placebo	Almorexant 100mg	Almorexant 200mg	Zolpidem 10mg	Total
Overall Participants [units: participants]	177	186	176	168	707
Age [units: participants]					
<=18 years	0	0	0	0	0
Between 18 and 65 years	177	186	176	168	707
>=65 years	0	0	0	0	0
Age [units: years] Mean (Standard Deviation)	46.2 (11.69)	44.1 (12.44)	46.1 (11.83)	45.1 (12.11)	45.4 (12.03)
Gender [units: participants]					

Female	**111**	**113**	**106**	**106**	**436**
Male	**66**	**73**	**70**	**62**	**271**
Region of Enrollment [units: participants]					
Australia	**13**	**15**	**12**	**14**	**54**
Austria	**3**	**5**	**2**	**4**	**14**
Belgium	**0**	**1**	**1**	**0**	**2**
Bulgaria	**1**	**0**	**1**	**0**	**2**
Czech Republic	**2**	**2**	**1**	**1**	**6**
Denmark	**6**	**5**	**5**	**4**	**20**
Finland	**13**	**14**	**13**	**14**	**54**
France	**3**	**2**	**3**	**2**	**10**
Germany	**83**	**86**	**87**	**81**	**337**
Hungary	**12**	**11**	**11**	**13**	**47**
Israel	**5**	**5**	**6**	**5**	**21**
Italy	**3**	**3**	**2**	**2**	**10**
Poland	**3**	**3**	**3**	**3**	**12**
South Africa	**15**	**13**	**13**	**12**	**53**
Spain	**4**	**6**	**5**	**3**	**18**
Sweden	**6**	**8**	**5**	**6**	**25**
Switzerland	**1**	**4**	**4**	**1**	**10**
United Kingdom	**4**	**3**	**2**	**3**	**12**

Outcome Measures

Hide All Outcome Measures

1. Primary: Change From Baseline to Day 1&2 in Wake After Sleep Onset (WASO) [Time Frame: From baseline to Day 1&2]

Measure Type	Primary
Measure Title	Change From Baseline to Day 1&2 in Wake After Sleep Onset (WASO)
Measure Description	WASO was defined as the time spent in epochs scored as wake after onset of persistent sleep as determined by polysomnography (PSG) until lights on. For WASO assessed at the study center, the mean of the 2 PSG nights at each of Visits 3 and 4 was used for Day 1&2 and Day 15&16
Time Frame	From baseline to Day 1&2
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.
All treated patients

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg

	zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Measured Values

	Placebo	Almorexant 100mg	Almorexant 200mg	Zolpidem 10mg
Overall Participants [units: participants]	**177**	**186**	**176**	**168**
Change From Baseline to Day 1&2 in Wake After Sleep Onset (WASO) [units: minutes] Median (95% Confidence Interval)				
Baseline	**85.0** **(77.3 to 91.0)**	**86.6** **(80.0 to 92.3)**	**92.3** **(84.8 to 98.3)**	**76.5** **(69.3 to 82.0)**
Day 1&2	**72.8** **(63.3 to 81.8)**	**54.5** **(47.3 to 61.0)**	**46.4** **(41.8 to 49.8)**	**54.6** **(49.0 to 62.5)**
Change from baseline to day 1&2	**-11.8** **(-19.3 to -7.3)**	**-29.0** **(-33.0 to -23.3)**	**-40.4** **(-47.5 to -31.5)**	**-17.9** **(-25.3 to -12.0)**

Statistical Analysis 1 for Change From Baseline to Day 1&2 in Wake After Sleep Onset (WASO)

Groups [1]	Placebo vs. Almorexant 100mg
Method [2]	Wilcoxon rank-sum
P Value [3]	<0.0001
Median Difference (Net) [4]	-15.0
95% Confidence Interval	-21.8 to -8.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change From Baseline to Day 1&2 in Wake After Sleep Onset (WASO)

Groups [1]	Placebo vs. Almorexant 200mg
Method [2]	Wilcoxon rank-sum
P Value [3]	<0.0001
Median Difference (Net) [4]	-26.8
95% Confidence Interval	-34.3 to -19.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:

	No text entered.

Statistical Analysis 3 for Change From Baseline to Day 1&2 in Wake After Sleep Onset (WASO)

Groups [1]	Placebo vs. Zolpidem 10mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0376
Median Difference (Net) [4]	-6.8
95% Confidence Interval	-13.5 to -0.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

2. Primary: Change From Baseline to Day 15&16 in WASO [Time Frame: From baseline to Day 15&16]

Measure Type	Primary
Measure Title	Change From Baseline to Day 15&16 in WASO
Measure Description	WASO was defined as the time spent in epochs scored as wake after onset of persistent sleep as determined by polysomnography (PSG) until lights on. For WASO assessed at the study center, the mean of the 2 PSG nights at each of Visits 3 and 4 was used for Day 1&2 and Day 15&16
Time Frame	From baseline to Day 15&16
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.
All treated patients

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Measured Values

	Placebo	Almorexant 100mg	Almorexant 200mg	Zolpidem 10mg
Overall Participants [units: participants]	**177**	**186**	**176**	**168**
Change From Baseline to Day 15&16 in WASO [units: minutes] Median (95% Confidence Interval)				
Baseline	**85.0** **(77.3 to 91.0)**	**86.6** **(80.0 to 92.3)**	**92.3** **(84.8 to 98.3)**	**76.5** **(69.3 to 82.0)**
Day 15&16	**65.0** **(56.0 to 71.5)**	**55.8** **(50.5 to 59.0)**	**51.8** **(46.3 to 56.0)**	**63.0** **(56.5 to 72.5)**
Change from baseline to Day 15&16	**-18.3** **(-22.0 to -12.0)**	**-29.6** **(-33.5 to -23.8)**	**-36.3** **(-43.8 to -26.5)**	**-15.1** **(-19.0 to -8.8)**

Statistical Analysis 1 for Change From Baseline to Day 15&16 in WASO

Groups [1]	Placebo vs. Almorexant 100mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0001
Median Difference (Net) [4]	-13.5
95% Confidence Interval	-20.3 to -6.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 15&16 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change From Baseline to Day 15&16 in WASO

Groups [1]	Placebo vs. Almorexant 200mg
Method [2]	Wilcoxon rank-sum
P Value [3]	<0.0001
Median Difference (Net) [4]	-19.5
95% Confidence Interval	-27.3 to -12.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 15&16 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change From Baseline to Day 15&16 in WASO

Groups [1]	Placebo vs. Zolpidem 10mg

Method [2]	Wilcoxon rank-sum
P Value [3]	0.3358
Median Difference (Net) [4]	3.5
95% Confidence Interval	-3.8 to 11.0

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 15&16 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

3. Primary: Change From Baseline to Week 1&2 in the Self-reported WASO (sWASO) [Time Frame: From baseline to Week 1&2]

Measure Type	Primary
Measure Title	Change From Baseline to Week 1&2 in the Self-reported WASO (sWASO)
Measure Description	sWASO was the self-reported time spent awake after sleep onset as reported in the sleep diary. For sWASO assessed at home, the mean of all available data collected between Visits 3 and 4 (i.e., after the second morning of Visit 3 and before the first evening of Visit 4) was used for Week 1&2
Time Frame	From baseline to Week 1&2
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.
All treated patients with available data

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Measured Values

	Placebo	**Almorexant 100mg**	**Almorexant 200mg**	**Zolpidem 10mg**
Overall Participants [units: participants]	**175**	**179**	**173**	**168**
Change From Baseline to Week 1&2 in the Self-reported WASO (sWASO)				

[units: minutes] Median (95% Confidence Interval)				
Baseline	**64.0 (60.0 to 75.0)**	**65.0 (59.5 to 72.0)**	**69.0 (63.0 to 77.0)**	**61.6 (55.0 to 70.9)**
Week 1&2	**52.9 (47.5 to 58.1)**	**40.5 (34.5 to 48.3)**	**42.9 (37.5 to 47.5)**	**30.5 (25.9 to 39.6)**
Change from baseline to week 1&2	**-14.1 (-20.0 to -9.2)**	**-19.5 (-22.9 to -12.7)**	**-21.8 (-28.8 to -17.5)**	**-23.4 (-27.5 to -19.0)**

Statistical Analysis 1 for Change From Baseline to Week 1&2 in the Self-reported WASO (sWASO)

Groups [1]	Placebo vs. Almorexant 100mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0186
Median Difference (Net) [4]	-7.3
95% Confidence Interval	-13.3 to -1.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to week 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change From Baseline to Week 1&2 in the Self-reported WASO (sWASO)

Groups [1]	Placebo vs. Almorexant 200mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0006
Median Difference (Net) [4]	-10.4
95% Confidence Interval	-16.4 to -4.6

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to week 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change From Baseline to Week 1&2 in the Self-reported WASO (sWASO)

Groups [1]	Placebo vs. Zolpidem 10mg
Method [2]	Wilcoxon rank-sum
P Value [3]	<0.0001

Median Difference (Net) [4]	-12.7
95% Confidence Interval	-18.8 to -6.6

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to week 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

4. Secondary: Change From Baseline to Day 1&2 in Latency to Persistent Sleep (LPS) [Time Frame: From baseline to Day 1&2]

Measure Type	Secondary
Measure Title	Change From Baseline to Day 1&2 in Latency to Persistent Sleep (LPS)
Measure Description	LPS was defined as the time from the start of the PSG recording to the beginning of the first continuous 20 epochs (i.e., 10 minutes) scored as non-wake (i.e., either sleep stage 1 (S1), sleep stage 2 (S2), slow-wave sleep (SWS), or rapid eye movement sleep(REM)) as determined by PSG
Time Frame	From baseline to Day 1&2
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.
All treated patients

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Measured Values

	Placebo	**Almorexant 100mg**	**Almorexant 200mg**	**Zolpidem 10mg**
Overall Participants [units: participants]	**177**	**186**	**176**	**168**
Change From Baseline to Day 1&2 in Latency to Persistent Sleep (LPS) [units: minutes] Median (95% Confidence Interval)				
Baseline	**57.3** **(53.0 to 65.5)**	**57.4** **(52.0 to 63.3)**	**54.1** **(47.5 to 58.3)**	**56.5** **(52.3 to 66.0)**

Day 1&2	**37.5 (32.3 to 44.0)**	**28.8 (25.0 to 34.5)**	**25.0 (22.3 to 28.3)**	**22.5 (20.3 to 26.8)**
Change from baseline to day 1&2	**-15.8 (-19.5 to -11.0)**	**-24.8 (-29.8 to -18.3)**	**-22.5 (-27.5 to -20.5)**	**-29.4 (-35.8 to -25.3)**

Statistical Analysis 1 for Change From Baseline to Day 1&2 in Latency to Persistent Sleep (LPS)

Groups [1]	Placebo vs. Almorexant 100mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0035
Median Difference (Net) [4]	-9.3
95% Confidence Interval	-15.3 to -3.0

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change From Baseline to Day 1&2 in Latency to Persistent Sleep (LPS)

Groups [1]	Placebo vs. Almorexant 200mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0006
Median Difference (Net) [4]	-9.5
95% Confidence Interval	-15.0 to -4.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change From Baseline to Day 1&2 in Latency to Persistent Sleep (LPS)

Groups [1]	Placebo vs. Zolpidem 10mg
Method [2]	Wilcoxon rank-sum
P Value [3]	<0.0001
Median Difference (Net) [4]	-16.0
95% Confidence Interval	-22.0 to -9.8

[1]	Additional details about the analysis, such as null hypothesis and power calculation:

	Change from baseline to day 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

5. Secondary: Change From Baseline to Day 15&16 in LPS [Time Frame: From baseline to Day 15&16]

Measure Type	Secondary
Measure Title	Change From Baseline to Day 15&16 in LPS
Measure Description	LPS was defined as the time from the start of the PSG recording to the beginning of the first continuous 20 epochs (i.e., 10 minutes) scored as non-wake (i.e., either sleep stage 1 (S1), sleep stage 2 (S2), slow-wave sleep (SWS), or rapid eye movement sleep(REM)) as determined by PSG
Time Frame	From baseline to Day 15&16
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.
All treated patients

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Measured Values

	Placebo	**Almorexant 100mg**	**Almorexant 200mg**	**Zolpidem 10mg**
Overall Participants [units: participants]	**177**	**186**	**176**	**168**
Change From Baseline to Day 15&16 in LPS [units: minutes] Median (95% Confidence Interval)				
Baseline	**57.3** **(53.0 to 65.5)**	**57.4** **(52.0 to 63.3)**	**54.1** **(47.5 to 58.3)**	**56.5** **(52.3 to 66.0)**
Day 15&16	**30.0** **(26.0 to 37.8)**	**29.3** **(25.8 to 35.3)**	**24.1** **(21.5 to 28.0)**	**24.6** **(21.3 to 28.3)**
Change from baseline to day 15&16	**-20.0** **(-25.8 to -16.3)**	**-23.5** **(-31.0 to -20.0)**	**-26.5** **(-30.8 to -22.8)**	**-32.3** **(-36.0 to -26.0)**

Statistical Analysis 1 for Change From Baseline to Day 15&16 in LPS

Groups [1]	Placebo vs. Almorexant 100mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.2237
Median Difference (Net) [4]	-4.0
95% Confidence Interval	-11.0 to 2.5

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 15&16 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change From Baseline to Day 15&16 in LPS

Groups [1]	Placebo vs. Almorexant 200mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0607
Median Difference (Net) [4]	-6.0
95% Confidence Interval	-12.3 to 0.3

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 15&16 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change From Baseline to Day 15&16 in LPS

Groups [1]	Placebo vs. Zolpidem 10mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0017
Median Difference (Net) [4]	-10.5
95% Confidence Interval	-17.3 to -4.0

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to day 15&16 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical

	significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

6. Secondary: Change From Baseline to Week 1&2 in Subjective Latency to Sleep Onset (sLSO) [Time Frame: From baseline to Week 1&2]

Measure Type	Secondary
Measure Title	Change From Baseline to Week 1&2 in Subjective Latency to Sleep Onset (sLSO)
Measure Description	sLSO was the self-reported time to fall asleep as reported in the sleep diary
Time Frame	From baseline to Week 1&2
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.
All treated patients with available data

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Measured Values

	Placebo	**Almorexant 100mg**	**Almorexant 200mg**	**Zolpidem 10mg**
Overall Participants [units: participants]	**175**	**179**	**173**	**168**
Change From Baseline to Week 1&2 in Subjective Latency to Sleep Onset (sLSO) [units: minutes] Median (95% Confidence Interval)				
Baseline	**58.8** **(52.0 to 64.5)**	**55.0** **(49.0 to 60.6)**	**53.3** **(50.5 to 58.4)**	**50.5** **(45.2 to 57.0)**
Week 1&2	**45.0** **(39.2 to 51.0)**	**36.5** **(32.9 to 41.7)**	**34.5** **(31.5 to 38.3)**	**33.3** **(31.1 to 37.2)**
Change from baseline to week 1&2	**-10.0** **(-15.1 to -4.7)**	**-16.2** **(-19.3 to -12.4)**	**-16.2** **(-19.9 to -13.5)**	**-17.2** **(-19.9 to -12.3)**

Statistical Analysis 1 for Change From Baseline to Week 1&2 in Subjective Latency to Sleep Onset (sLSO)

Groups [1]	Placebo vs. Almorexant 100mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.1187

Median Difference (Net) [4]	-4.1
95% Confidence Interval	-9.1 to 0.9

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to week 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 2 for Change From Baseline to Week 1&2 in Subjective Latency to Sleep Onset (sLSO)

Groups [1]	Placebo vs. Almorexant 200mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0017
Median Difference (Net) [4]	-7.1
95% Confidence Interval	-11.5 to -2.7

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to week 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Statistical Analysis 3 for Change From Baseline to Week 1&2 in Subjective Latency to Sleep Onset (sLSO)

Groups [1]	Placebo vs. Zolpidem 10mg
Method [2]	Wilcoxon rank-sum
P Value [3]	0.0121
Median Difference (Net) [4]	-6.1
95% Confidence Interval	-10.8 to -1.4

[1]	Additional details about the analysis, such as null hypothesis and power calculation:
	Change from baseline to week 1&2 compared with placebo
[2]	Other relevant method information, such as adjustments or degrees of freedom:
	No text entered.
[3]	Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
	No text entered.
[4]	Other relevant estimation information:
	No text entered.

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	All adverse events occurring after the start of study treatment and within 24 hours after the last dose of study treatment
Additional Description	No text entered.

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Serious Adverse Events

	Placebo	**Almorexant 100mg**	**Almorexant 200mg**	**Zolpidem 10mg**
Total, serious adverse events				
# participants affected / at risk	**0/177 (0.00%)**	**2/186 (1.08%)**	**1/176 (0.57%)**	**0/168 (0.00%)**
Infections and infestations				
ABSCESS LIMB † 1				
# participants affected / at risk	**0/177 (0.00%)**	**1/186 (0.54%)**	**0/176 (0.00%)**	**0/168 (0.00%)**
# events	**0**	**1**	**0**	**0**
Nervous system disorders				
MULTIPLE SCLEROSIS † 1				
# participants affected / at risk	**0/177 (0.00%)**	**1/186 (0.54%)**	**0/176 (0.00%)**	**0/168 (0.00%)**
# events	**0**	**1**	**0**	**0**
Renal and urinary disorders				
CALCULUS URETERIC † 1				
# participants affected / at risk	**0/177 (0.00%)**	**0/186 (0.00%)**	**1/176 (0.57%)**	**0/168 (0.00%)**
# events	**0**	**0**	**1**	**0**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (12.0)

Other Adverse Events

Hide Other Adverse Events

Time Frame	All adverse events occurring after the start of study treatment and within 24 hours after the last dose of study treatment
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	1

Reporting Groups

	Description
Placebo	Placebo Placebo : 2 placebo matching almorexant tablets and 1 placebo matching over-encapsulated zolpidem
Almorexant 100mg	almorexant 100 mg almorexant : 1 100 mg almorexant tablet, 1 placebo matching almorexant tablet, and 1 placebo matching over-encapsulated zolpidem
Almorexant 200mg	almorexant 200 mg almorexant : 2 100 mg almorexant tablets, and 1 placebo matching over-encapsulated zolpidem
Zolpidem 10mg	zolpidem 10 mg zolpidem : 2 placebo matching almorexant tablets and 1 zolpidem 10 mg over-encapsulated

Other Adverse Events

	Placebo	Almorexant 100mg	Almorexant 200mg	Zolpidem 10mg
Total, other (not including serious) adverse events				
# participants affected / at risk	**64/177 (36.16%)**	**65/186 (34.95%)**	**61/176 (34.66%)**	**72/168 (42.86%)**
Cardiac disorders				
PALPITATIONS † [1]				
# participants affected / at risk	**1/177 (0.56%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**2/168 (1.19%)**
Ear and labyrinth disorders				
VERTIGO † [1]				
# participants affected / at risk	**0/177 (0.00%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**2/168 (1.19%)**
Eye disorders				
BLEPHAROSPASM † [1]				
# participants affected / at risk	**0/177 (0.00%)**	**0/186 (0.00%)**	**2/176 (1.14%)**	**0/168 (0.00%)**
VISION BLURRED † [1]				
# participants affected / at risk	**3/177 (1.69%)**	**0/186 (0.00%)**	**1/176 (0.57%)**	**1/168 (0.60%)**
Gastrointestinal disorders				
NAUSEA † [1]				
# participants affected / at risk	**7/177 (3.95%)**	**4/186 (2.15%)**	**6/176 (3.41%)**	**4/168 (2.38%)**
DIARRHOEA † [1]				
# participants affected / at risk	**1/177 (0.56%)**	**6/186 (3.23%)**	**1/176 (0.57%)**	**2/168 (1.19%)**
ABDOMINAL PAIN UPPER † [1]				
# participants affected / at risk	**3/177 (1.69%)**	**3/186 (1.61%)**	**2/176 (1.14%)**	**1/168 (0.60%)**
CONSTIPATION † [1]				
# participants affected / at risk	**0/177 (0.00%)**	**2/186 (1.08%)**	**0/176 (0.00%)**	**0/168 (0.00%)**
DRY MOUTH † [1]				
# participants affected / at risk	**1/177 (0.56%)**	**1/186 (0.54%)**	**0/176 (0.00%)**	**3/168 (1.79%)**
DYSPEPSIA † [1]				
# participants affected / at risk	**2/177 (1.13%)**	**0/186 (0.00%)**	**1/176 (0.57%)**	**1/168 (0.60%)**
General disorders				
FATIGUE † [1]				
# participants affected / at risk	**2/177 (1.13%)**	**9/186 (4.84%)**	**6/176 (3.41%)**	**6/168 (3.57%)**
ASTHENIA † [1]				
# participants affected / at risk	**2/177 (1.13%)**	**5/186 (2.69%)**	**3/176 (1.70%)**	**1/168 (0.60%)**
CHEST DISCOMFORT † [1]				
# participants affected / at risk	**1/177 (0.56%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**1/168 (0.60%)**
Infections and infestations				
NASOPHARYNGITIS † [1]				
# participants affected / at risk	**3/177 (1.69%)**	**5/186 (2.69%)**	**2/176 (1.14%)**	**5/168 (2.98%)**
INFLUENZA † [1]				
# participants affected / at risk	**0/177 (0.00%)**	**2/186 (1.08%)**	**0/176 (0.00%)**	**0/168 (0.00%)**

Investigations				
WEIGHT INCREASED † 1				
# participants affected / at risk	**0/177 (0.00%)**	**0/186 (0.00%)**	**3/176 (1.70%)**	**1/168 (0.60%)**
Metabolism and nutrition disorders				
FOOD CRAVING † 1				
# participants affected / at risk	**0/177 (0.00%)**	**0/186 (0.00%)**	**2/176 (1.14%)**	**0/168 (0.00%)**
Musculoskeletal and connective tissue disorders				
MUSCLE SPASMS † 1				
# participants affected / at risk	**2/177 (1.13%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**0/168 (0.00%)**
Nervous system disorders				
HEADACHE † 1				
# participants affected / at risk	**21/177 (11.86%)**	**18/186 (9.68%)**	**26/176 (14.77%)**	**29/168 (17.26%)**
DIZZINESS † 1				
# participants affected / at risk	**10/177 (5.65%)**	**6/186 (3.23%)**	**8/176 (4.55%)**	**3/168 (1.79%)**
SOMNOLENCE † 1				
# participants affected / at risk	**4/177 (2.26%)**	**6/186 (3.23%)**	**5/176 (2.84%)**	**4/168 (2.38%)**
BALANCE DISORDER † 1				
# participants affected / at risk	**0/177 (0.00%)**	**1/186 (0.54%)**	**2/176 (1.14%)**	**2/168 (1.19%)**
DYSGEUSIA † 1				
# participants affected / at risk	**1/177 (0.56%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**3/168 (1.79%)**
PARAESTHESIA † 1				
# participants affected / at risk	**2/177 (1.13%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**2/168 (1.19%)**
Psychiatric disorders				
DEPRESSED MOOD † 1				
# participants affected / at risk	**0/177 (0.00%)**	**2/186 (1.08%)**	**1/176 (0.57%)**	**3/168 (1.79%)**
CONFUSIONAL STATE † 1				
# participants affected / at risk	**1/177 (0.56%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**2/168 (1.19%)**
NIGHTMARE † 1				
# participants affected / at risk	**2/177 (1.13%)**	**0/186 (0.00%)**	**2/176 (1.14%)**	**1/168 (0.60%)**
ANXIETY † 1				
# participants affected / at risk	**0/177 (0.00%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**2/168 (1.19%)**
RESTLESSNESS † 1				
# participants affected / at risk	**0/177 (0.00%)**	**0/186 (0.00%)**	**2/176 (1.14%)**	**0/168 (0.00%)**
Renal and urinary disorders				
MICTURITION URGENCY † 1				
# participants affected / at risk	**0/177 (0.00%)**	**1/186 (0.54%)**	**1/176 (0.57%)**	**0/168 (0.00%)**
Respiratory, thoracic and mediastinal disorders				
OROPHARYNGEAL PAIN † 1				
# participants affected / at risk	**1/177 (0.56%)**	**2/186 (1.08%)**	**0/176 (0.00%)**	**2/168 (1.19%)**
COUGH † 1				
# participants affected / at risk	**1/177 (0.56%)**	**0/186 (0.00%)**	**1/176 (0.57%)**	**2/168 (1.19%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA (12.0)

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
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: No text entered.

Results Point of Contact:

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Responsible Party:	Midnight Pharma, LLC
ClinicalTrials.gov Identifier:	NCT00608985 History of Changes
Other Study ID Numbers:	**AC-057A301**
Study First Received:	January 11, 2008
Results First Received:	December 21, 2012
Last Updated:	February 11, 2016
Health Authority:	Poland: Ministry of Health Switzerland: Swissmedic Czech Republic: State Institute for Drug Control Finland: Finnish Medicines Agency Germany: Federal Institute for Drugs and Medical Devices Denmark: Danish Medicines Agency South Africa: Medicines Control Council Hungary: National Institute of Pharmacy France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Australia: Department of Health and Ageing Therapeutic Goods Administration Israel: Ministry of Health Belgium: Federal Agency for Medicinal Products and Health Products Italy: The Italian Medicines Agency Sweden: Medical Products Agency Bulgaria: Bulgarian Drug Agency Spain: Ministry of Health United Kingdom: Medicines and Healthcare Products Regulatory Agency