Table 7.2.5.1 Investigators and Sites for study 308	
B. Adam, MD (30853) n = 4 45 Boulevard de l'Yser 76000 Rouen (France)	J. Boulenge, MD (30859) n = 2 102 Rue Méridienne 76100 Rouen (France)
M. Alder, MD (30814) n = 9 Belmont Health Centre 510 Kenton Lane, Harrow Middlesex HA3 7LT (U. K.)	A. Campagne, MD (30822) n = 24 81 Rue Blaise Pascal 37000 Tours (France)
M- L. Alin, MD (30803) n = 10 Geriatriska Kliniken Sabbatsberg sjukhus, Box 6406 11382 Stockholm (Sweden)	F. Cañellas, MD (30827) n = 7 Hospital Son Dureta c/ Andrea Doria, s/ n 07014 Palma de Mallorca (Spain)
D. Backhaus, MD (30842) n =15 Ärtzin für Neurologie und Psychiatrie Bahnofsplatz 5 31134 Hildesheim (Germany)	B. Cauchois, MD (30850) n = 11 Cabinet des Floralies, 6 Rue Poitron 76000 Rouen (France)
P. Beignot- Devalmont, MD (30858) n = 6 102 Rue Méridienne 76100 Rouen (France)	F. Cirignotta, MD (30806) n = 1 Servizio di Neurologia Azienda Ospedaliera di Bologna Policlinico Sant'Orsola- Malpighi Via Albertoni 15, 40138 Bologna (Italy)
E. Blot, MD (30820) n = 9 45 Boulevard de l'Yser 76000 Rouen (France)	J -P. Dehaye, MD (30876) n = 4 Résidence Ste Gertrude 23 a Rue des Capucins 1000 Bruxelles (Belgium)
M. Bongaerts, MD (30844) n = 5 48 Max Elskampstraat 2020 Antwerpen (Belgium)	P. De La Belliere, MD (30821) n = 12 Centre commercial du Chapitre Avenue Georges Pompidou 76420 Bihorel (France)
D. Delbecq, MD (30878) n = 5 40 Rue du Faubourg Montmartre 75009 Paris (France)	H. Herrmann, MD (30841) n = 47 Parexel Berlin, Spandauer Damm 130 14050 Berlin (Germany)
S. De Risio, MD (30867) n = 6 Institute di Psichiatria Policlinico "A. Gemelli", Largo Gemelli 1 Roma (Italy)	P. Hurtebize, MD (30863) n = 10 Place de l'Eglise 76190 Allouville- Bellefosse (France)
B. Dietrich, MD (30834) n = 44 L. A. B GmBH & Co Wegenerstrasse 13 89231 Neu- Ulm (Germany)	C. Hwang, MD (30879) n = 6 44 Avenue de Versailles 75016 Paris (France)
M. Dreyfuss, MD (30870) n = 9 38 Rue Poussin 75016 Paris (France)	J- C. Jamot, MD (30836) n = 3 10 Rue Benoît Malon 76300 Sotteville- les- Rouen (France)
J. Espinar- Sierra, MD (30831) n = 2 Hospital universitario San Carlos Dpt neurofisiologia clinica c/ Prof Martin Lagos, s/ n 28040 Madrid (Spain)	H. A. C. Kamphuisen, MD (30805) n = 6 Centrum voor Slaap- waakstoornissen Westeinde Ziekenhuis, Lijnbaan 32 2512 Van Den Haag (Netherlands)
E. Estivill, MD (30826) n = 12 Dexeus Institute, Sleep disorders unit Paseo Bonanova, 61 bajos 08017 Barcelona (Spain)	P. Lemaire, MD (30846) n = 4 29 Rue du Lac 1050 Bruxelles (Belgium)
	A. Louis, MD (30877) n = 4 Fondations Réunies, 45 Rue des Alexiens 1000 Bruxelles (Belgium)

Table 7.2.5.1 Investigators and Sites for study 308	
N. Gostick, MD (30813) n = 1 Central Surgery research unit Corporation Street, Rugby Warwickshire CV 21 3SP (U. K.)	M. Lundberg, MD (30804) n = 5 Måsens VC, Örnvägen 28 22732 Lund (Sweden)
J. Hedner, MD (30828) n = 43 Avd. 70, Sömnlab, Lungdivisionen Kvinnokliniken / 4th floor Sahlgrenska sjukhuset, Blåstråket 6 41345 Göteborg (Sweden)	S. K. Mahanty, MD (30818) n = 6 8 Pinders Grove, Wakefield West Yorkshire WF1 4AH (U. K.)
K- H. Molz, MD (30871) n = 22 Apex Research, Landsbergerstrasse 476 81241 München (Germany)	A. Richens, MD (30816) n = 3 Cardiff Clinical Trials Limited University of Wales College of Medicine, Health Park Cardiff CF4 4XN (U. K.)
L. Murri, MD (30807) n = 2 U. D. Neurofisiopatologia Università degli studi di Pisa Ospedale Santa Chiara Via Roma 67, Pisa (Italy)	L. Rodriguez, MD (30829) n = 2 Hospital Universitario de Getafe Ctra Toledo, km 12 500 28905 Getafe (Spain)
J. Ortiz, MD (30833) n = 1 Hospital Gregorio Marañon c/ Dtor Esquerdo 46 28007 Madrid (Spain)	T. Sagales, MD (30830) n = 6 S. Neurofisiologia Clinica Hospital Universitario Vall Hebròn 08035 Barcelona (Spain)
S. Pavie- Houdry, MD (30872) n = 1 9 Rue de Civry 75016 Paris (France)	J. Saiz, MD (30832) n = 1 Hospital Ramon y Cajal Ctra. Colmenar, km 9,1 28037 Madrid (Spain)
F. Puca, MD (30865) n = 3 Università degli Studi di Bari Clinica Neurologica II Policlinico Via G. Cesare 70100 Bari (Italy)	K. Schaffler, MD (30838) n = 9 Institute für Pharmakodynamische Forschung Kronstadter Strasse 5 81677 München (Germany)
D. Rabaud, MD (30823) n = 12 Cabinet médical St Clément 102 Rue Méridienne 76000 Rouen (France)	H- J. Schietsch, MD (30843) n = 2 Theodor- Heuss- Platz 1 Augsburg (Germany)
S. Regenberg, MD (30801) n = 8 Hauptstrasse 277 33818 Leopoldshöhe (Germany)	G. Sjönell, MD (30839) n = 2 Kvartersakuten Matteus Norrtullsgatan 12B, 6tr 11327 Stockholm (Sweden)
J. Reuss, MD (30825) n = 11 Residencia Asistida de Manoteras c/ OÑA 3, Madrid (Spain)	H. W. Spiess, MD (30861) n = 2 102 Rue Méridienne 76100 Rouen (France)
M. Stolt, MD (30840) n = 1 Kvartersakuten Vasastan Norrtullsgatan 10, 1tr 11327 Stockholm (Sweden)	R. Yaeche, MD (30819) n = 14 10 Rue Benoît Malon 76300 Sotteville- les- Rouen (France)
P. Vinnal, MD (30802) n = 3 Luthagens VC, Geijersgatan 8 Sabbatsberg Sjukhus, Box 6406 11382 Stockholm (Sweden)	APPEARS THIS WAY ON ORIGINAL

Table 7.2.5.2 Scedule of assessments and procedures for study 308

Procedures	Period	Initial Screening	Single- Blind Placebo Run- in		Randomized Double- blind Treatment					Single- Blind Placebo / Run- out	Follow- up* / Final or Re- evaluation
Dose	Night :	-28 to -8	-7	-6 to -1	1	2 to 7	8	9 to 14	+1	+2 to +7	+8 to +11
Study		-28 to -8	-7	-6 to -1	1	2 to 7	8	9 to 14	15	16 to 21	22 to 25
Medical history		X									
Eligibility		X	X		X						
Zung A& D; psychiatric interview		X									
Signed informed consent		X									
Prior CNS medication washout		X									
Physical examination		X									X
Interim physical examination			X		X		X		X		
Vital signs		X	X		X		X		X		X
Impairment assessment		X	X		X		X		X		X
Standard ECG		X									X
Clinical labs		X	X		X				X		X
Urine drug screen (UDS)		X	X						X		
Patient daily diary			X	X	X	X	X	X	X	X	X
Presleep questionnaire			X	X	X	X	X	X	X	X	X
Postsleep questionnaire			X	X	X	X	X	X	X	X	X
Compliance check (drug, diaries and questionnaires)					X		X		X		
Single- blind placebo dose			X	X					X	X	
administration											
Double- blind dose administration					X	X	X	X			
Study events			X	X	X	X	X	X	X	X	X

*Procedure performed at final visit for early drop-outs.

Table 7.2.5.4 OBSERVED CASE ANALYSIS (308-EU) X=Median time to sleep onset (minutes) ITT patients.

Treatment Groups	Treatment Week					
	Baseline		Wk 1		Wk 2	
	n	X	n	X	n	X
Zaleplon 5 mg	139	62.1	139	43.1	129	39.3
Zaleplon 10 mg	145	70.7	145	40.0	139	36.4
PLACEBO	138	68.0	137	60.0	136	49.3
p-values for zaleplon Dunnett's test Control=placebo						
Zaleplon 5 mg vs Placebo			.001		<.001	
Zaleplon 10 mg vs Placebo			<.001		<.001	

Table 7.2.5.5 LOCF ANALYSIS (308-EU) X=Median time to sleep onset (minutes) ITT patients.

Treatment Groups	Treatment Week					
	Baseline		Wk 1		Wk 2	
	n	X	n	X	n	X
Zaleplon 5 mg	139	62.1	139	43.1	139	40.0
Zaleplon 10 mg	145	70.7	145	40.0	145	37.1
PLACEBO	138	68.0	137	60.0	138	49.6
p-values for zaleplon Dunnett's test Control=placebo						
Zaleplon 5 mg vs Placebo			.001		<.001	
Zaleplon 10 mg vs Placebo			<.001		<.001	

Table 7.2.5.6 OBSERVED CASE ANALYSIS (308-EU) X=Median total time slept (minutes) ITT patients

Treatment Groups	Treatment Week					
	Baseline		Wk 1		Wk 2	
	n	X	n	X	n	X
Zaleplon 5 mg	139	325.7	139	342.0	129	351.7
Zaleplon 10 mg	145	304.3	145	342.9	139	351.4
PLACEBO	138	322.0	138	346.1	136	342.9
p-values for zaleplon Dunnett's test Control=placebo						
Zaleplon 5 mg vs Placebo			.58		.72	
Zaleplon 10 mg vs Placebo			.04		.22	

Table 7.2.5.7 OBSERVED CASE ANALYSIS (308-EU) X=Median (mean) number of awakenings ITT patients

Treatment Groups	Treatment Week					
	Baseline		Wk 1		Wk 2	
	n	X	n	X	n	X
Zaleplon 5 mg	138	2 (2.2)	137	2 (2.0)	124	2 (2.0)
Zaleplon 10 mg	141	2 (2.4)	142	2 (1.9)	135	2 (2.2)
PLACEBO	137	2 (2.0)	136	2 (1.8)	126	2 (1.7)
p-values for zaleplon Dunnett's test Control=placebo						
Zaleplon 5 mg vs Placebo			.21		.06	
Zaleplon 10 mg vs Placebo			.02		.07	

Table 7.2.6.1.1 Investigators in study 210-US. (Site number) (n at that site)
C. William Erwin, MD (21035) (n = 102) Duke University Medical Center Trent Drive Duke Hospital South Durham, NC, US 27710
Thomas Roth, PhD (21036) (n = 28) Sleep Disorders and Research Center Henry Ford Hospital One Ford Place, Suite 1D Detroit, MI, US 48202
Gerald Vogel, MD (21037) (n = 91) Sleep Research Laboratory, Inc. 1970 Cliff Valley Way NE, Ste 230 Atlanta, GA, US 30329
Gary K. Zammit, PhD (21038) (n = 46) Sleep Disorders Institute St. Luke's/ Roosevelt Hospital Center 1090 Amsterdam Avenue New York, NY, US 10025

Table 7.2.6.1.2 Scedule of events for study 210-US			
	Initial Screening	Evening	Next Morning
Procedure	(Day -21 to -10)	Night 1	Day 2
Medical and Psychiatric History	X		
Eligibility (7- night sleep diary)	X		
Signed Informed Consent	X		
Physical Examination	X		
Exit Physical Examination (Interim)			X
Vital Signs a	X	X	X
Weight	X	X	
Brief Neurologic Assessment	X	X	X
12- lead ECG	X		
Clinical Laboratory Determinations b	X		
Urine Drug Screen	X		
Pregnancy Tests (if applicable)			
Serum	X		
Urine		X	
Memory Tests c		X	X
Digit Symbol Substitution Test		X	X
Study Drug Administration		X	
(Randomization)			
PSG Recording		X	
Postsleep Questionnaire			X
Prior/ Concomitant Medication	X	X	X
Recording			
Study Events Recording		X	X
Discharge from Study			X

a: Vital signs include oral or tympanic temperature, respiratory rate, 5- minute sitting blood pressure (manual) and pulse.

b: Clinical laboratory determinations included hematology with differential blood count, blood chemistry, and urinalysis.

c: Test results were not captured in the case report form.

Table 7.2.6.1.3 Baseline demographics for subjects in study 210-US.					
	Placebo	Zaleplon 5 mg	Zaleplon 10 mg	Total	
Characteristic	(n = 89)	(n = 88)	(n = 90)	(n = 267)	p- Value
Sex, No. (%)					0.016 a
Men	40 (44.9)	26 (29.5)	23 (25.6)	89 (33.3)	
Women	49 (55.1)	62 (70.5)	67 (74.4)	178 (66.7)	
Age, years					0.69 b
Mean	36.2	36.3	36.8	36.4	
SD	9.6	8.7	9.2	9.1	
Range	26 - 59	25 - 58	26 - 60	25- 60	
Ethnic origin,					0.95 a
No. (%)					
Asian	2 (2.2)	2 (2.3)	2 (2.2)	6 (2.2)	
Black	17 (19.1)	18 (20.5)	19 (21.1)	54 (20.2)	
Hispanic	2 (2.2)	1 (1.1)	0 (0)	3 (1.1)	
White	68 (76.4)	67 (76.1)	69 (76.7)	204 (76.4)	
Weight, kg c					
Mean	72.4	70.3	68.7	70.5	0.056 b
SD	13.64	11.9	13.0	12.9	
Range	48.1 - 105.2	47.2 - 96.2	43.1 - 111.1	43.1 - 111.1	

a: Treatment groups were compared by using Fisher's Exact Test.

b: Treatment groups were compared by using ANOVA.

c: n = 87 for weight in zaleplon 5 mg group and total n = 266.

APPEARS THIS WAY ON ORIGINAL

Table 8.1.2 Serious adverse events occuring during the zaleplon development program

DRUG/ DOSE AT ONSET Study/ Patient ID Number	Age (y)	Sex	Time of Onset (Relative Days)	Serious Adverse Event
ZALEPLON 2 mg				
20732- 1431	71	F	2	Ventricular tachycardia, supraventricular tachycardia
ZALEPLON 5 mg				
20520- 0042	27	F	3	Nausea, dizziness, sweating
30309- 0471	53	M	29	Pericarditis
30608- 5287	76	M	13	Syncope
30608- 5576	82	M	13 OL	Skin carcinoma
30610- 5328	72	F	6 OL	Accidental Injury
30615- 5403	73	M	34 OL	Cerebral ischemia, liver function tests abnormal
30616- 5316	69	F	39 OL	Knee surgery
30625- 5731	65	F	12	Neoplasm
30626- 5229	67	F	15 OL	Carcinoma intestine
30627- 5130	71	F	13 OL	Breast neoplasm
30628- 5176	73	F	188 OL	Chest pain, ventricular extrasystoles, premature atrial contractions, asthma
30629- 5069	66	M	111 OL	Hip surgery
30630- 5009	84	F	112 OL	Abdominal pain
30636- 5562	72	F	99 OL	Breast neoplasm
30641- 5529	71	F	15	Abdominal pain, electrocardiogram abnormal, liver function tests abnormal
30643- 5510	68	F	30 OL	Liver function tests abnormal
30643- 5608	70	M	6	Accidental injury, hemothorax, pneumothorax
30825- 0338	76	M	3 OL	Abdominal pain, flatulence
30825- 0341	87	F	28 OL	Bundle branch block, ventricular tachycardia
30828- 0919	76	F	51 OL	Hernia
30838- 0121	72	M	1	Angina pectoris, cyanosis
30870- 0002	66	F	2	Malaise
ZALEPLON 10 mg				
20110- 1048	47	F	29	Hallucinations
20429- 0014	21	F	08	Hallucinations
20515- 0026	42	F	03	Incoordination, speech disorder, confusion, abnormal gait
20521- 0164	30	F	11	Unintended pregnancy

Table 8.1.2 Serious adverse events occuring during the zaleplon development program

DRUG/ DOSE AT ONSET Study/ Patient ID Number	Age (y)	Sex	Time of Onset (Relative Days)	Serious Adverse Event
20730- 1452	64	F	08	Confusion
30106- 4483	38	F	21	Unintended pregnancy, abortion
30110- 4781	26	F	14	Unintended pregnancy
30118- 4107	60	F	32	Surgical procedure, elective surgery, anemia
30207- 4559	60	F	40	Skin carcinoma
30211- 4541	43	F	99	Surgical procedure
30217- 4229	33	F	69	Bronchitis
30230- 4493	39	F	29	Intentional overdose
30231- 4190	33	F	112	Accidental injury, surgical procedure
30232- 4377	24	M	71	Glomerulitis
30319- 0229	35	M	03	Amnesia, thinking abnormal
30348- 0061	53	M	11	Hostility
30416- 0684	50	F	287	Cholelithiasis
30417- 0697	63	F	16	Abdominal pain
30419- 0529	57	F	273	Depression, goiter, bundle branch block
30610- 5080	68	M	88	Chest pain, dyspnea
30610- 5326	72	F	77 OL	Accidental injury, angina pectoris, electrocardiogram abnormal
30615- 5092	68	M	72	Pyelonephritis
30616- 5199	76	M	46	GI Neoplasia
30617- 5146	69	M	156 OL	Kidney pain, bundle branch block
30617- 5357	72	M	153 OL	Chest pain
30617- 5359	76	M	69 OL	Abdominal pain, surgical procedure
30618- 5047	72	M	321 OL	Accidental injury
30619- 5250	67	M	2	AV block, angina pectoris, pacemaker insertion
30620- 5162	75	F	52 OL	Coronary artery disorder, surgical procedure
30627- 5346	71	M	136 OL	Prostatic disorder, surgical procedure (post study)
30628- 5179	68	M	14	Bigeminy
30628- 5461	65	F	197 OL	Accidental injury
30630- 5003	70	F	190 OL	Cerebral ischemia, arterial anomaly, surgical procedure
30630- 5010	79	M	194 OL	Skin carcinoma
30630- 5623	75	F	18 OL	Non- specified drug reaction

Table 8.1.2 Serious adverse events occuring during the zaleplon development program

DRUG/ DOSE AT ONSET Study/ Patient ID Number	Age (y)	Sex	Time of Onset (Relative Days)	Serious Adverse Event
30632- 5102	69	M	395 OL	Surgical procedure, repair of abdominal aneurysm, post-study
30632- 5106	68	M	249 OL	Accidental injury, ankle fracture
30636- 5566	72	M	24 OL	Kidney calculus
30640- 5495	76	M	60 OL	Kidney calculus
30641- 5524	80	M	138 OL	Intestinal obstruction
30710- 0007	20	F	7	Hallucinations
30716- 0046	61	M	8	Arrhythmia
30716- 0053	28	F	23	Abdominal syndrome acute
30716- 0054	22	F	5	Syncope
30717- 0010	47	M	20	Hospitalization
30725- 0026	50	F	12	Chest pain, tachycardia, dyspnea
30801- 0033	76	F	4	Hallucinations
30818- 0715	74	F	10 OL	Vaginal hemorrhage
30822- 0010	74	M	124 OL	Asthenia
30822- 0018	87	M	81 OL	Pleural effusion
30823- 0008	71	F	82 OL	Cataract specified
30850- 0003	83	F	10	Accidental injury
30870- 0001	87	F	15 OL	Carcinoma of the Lung
31233- 0023	60	F	67	Accidental injury
31249- 0001	42	F	27	Uterine neoplasm, surgical procedure
ZALEPLON 20 mg				
20419- 0119	30	F	06	Hallucinations
20429- 0011	29	M	08	Depression
20429- 0013	21	F	03	Hallucinations, confusion, depression
20430- 0071	30	F	02	Amnesia
20732- 1430	60	M	50	Bundle branch block
30105- 4071	39	M	07	Dizziness, accidental injury
30130- 4710	36	F	12	Unintended pregnancy
30325- 0271	42	F	01	Muscle twitching, vertigo, visual disturbances
30709- 0003	39	F	12	Chest pain
30715- 0005	52	M	16	Amnesia, depersonalization
30738- 0014	25	F	12	Hallucinations
31218- 0006	26	F	53	Amnesia
31224- 0004	30	F	52	Abdominal pain
31227- 0009	44	F	47	Syncope

Table 8.1.2 Serious adverse events occuring during the zaleplon development program				
DRUG/ DOSE AT ONSET Study/ Patient ID Number	Age (y)	Sex	Time of Onset (Relative Days)	Serious Adverse Event
31228- 0001	43	F	30	Hepatitis, liver function tests abnormal
31230- 0002	24	F	175	Hallucinations
31230- 0003	39	M	187	Kidney calculus
31233- 0005	44	F	15	Amnesia
31238- 0008	28	F	79	Gastroenteritis
31245- 0005	58	M	117	Surgical procedure
31246- 0003	36	M	36	Gastritis
31252- 0004	55	F	49	Pulmonary embolus
ZALEPLON 40 mg				
20109- 1039	49	F	16	Amnesia
ZALEPLON 60 mg				
20208- 1104	24	M	15	Hallucinations
20208- 1110	44	F	08	Hallucinations
20209- 1125	60	F	29	Hallucinations
20209- 2140	29	M	08	Syncope
ZALEPLON dose unknown/ NA				
31228- 0003	46	F	34	Amnesia
31230- 0010	2½	M	1	Unintentional overdose
PLACEBO				
30120- 4217	24	F	6	Vaginal hemorrhage
30121- 4315	61	M	9	Trauma
30127- 4157	20	F	36	Unintended pregnancy
30609- 5331	73	F	28	Facial paralysis
30610- 5075	67	F	7	Cataract surgery
30620- 5161	74	M	7	Arteriosclerosis, angioplasty
30623- 5053	65	M	20	Bundle branch block
30628- 5178	66	M	6	Syncope, electrocardiogram abnormal
30639- 5486	71	F	17	Pain, dyspepsia
30708- 0005	49	M	6	Hostility
30721- 0008	42	M	5	Accidental injury, surgical procedure
30729- 0002	20	F	2	Sleep disorder
30740- 0007	36	F	20	Electrocardiogram abnormal, surgical procedure
30834- 0096	72	M	2	Angina pectoris, tachycardia
30841- 0110	73	M	11	Abdominal syndrome acute
PLACEBO RUN- OUT (assigned study drug/ dose)				
30621- 5206 (zaleplon 5 mg)	83	F	15	Urticaria

Table 8.1.2 Serious adverse events occuring during the zaleplon development program

DRUG/ DOSE AT ONSET Study/ Patient ID Number	Age (y)	Sex	Time of Onset (Relative Days)	Serious Adverse Event
30627- 5350 (zolpidem 10 mg)	64	M	67 OL	Possible myocardial infarction, anemia, accidental injury
30641- 5682 (zaleplon 10 mg)	65	M	20	Intestinal obstruction
30820- 0004 (zaleplon 5 mg)	70	F	12	Hallucinations
30825- 0339 (zaleplon 5 mg)	86	F	21	Cerebrovascular accident
30826- 0299 (placebo)	70	M	20	Fever, asthma
30829- 0355 (placebo)	91	M	22	Chest pain
ZOLPIDEM 5 mg				
30631- 5153	65	F	6	Angina pectoris,
				electrocardiogram abnormal
30634- 5270	70	M	8	Skin carcinoma
ZOLPIDEM 10 mg				
20420- 0038	31	M	13	Amnesia
20423- 0126	24	M	12	Hallucinations
30105- 4336	48	F	19	Amnesia
30309- 0475	54	F	17	Ataxia, vertigo, dizziness
30346- 0738	48	M	18	Dyspnea
TRIAZOLAM 0.25 mg				
20209- 1128	25	M	30	Hallucinations
20333- 3103	51	M	2	Hallucinations
POSTSTUDY (assigned study drug/ dose)				
30107- 4050 (zaleplon 20 mg)	60	F	12	Supraventricular tachycardia, atrial flutter
30707- 0015* (placebo/ zaleplon 10 mg/ zaleplon 20 mg/ placebo)	36	M	21	Liver function tests abnormal
30713- 0015 (placebo/ zaleplon 10 mg /zaleplon 20 mg/ placebo)	60	F	25	Electrocardiogram abnormal
30716- 0005 (placebo/ zaleplon 10 mg /zaleplon 10 mg/ placebo)	28	F	19	Unintended pregnancy
30720- 0007 (placebo/ zaleplon 10 mg /zaleplon 20 mg/ placebo)	52	F	22	Bigeminy

APPEARS THIS WAY ON ORIGINAL

Table 8.1.2.1 Halucinations occuring in zaleplon phase II/III development program

Patient Number	Age (y)	Sex	Dose at Onset	Adverse Event	Duration of Event	Relevance to Dose	Drug Relationship (Per Investigator)
20110- 1048	47	F	Zaleplon 10 mg	Hallucinations	45 min	After taking zaleplon	Related
20429- 0014	21	F	Zaleplon 10 mg	Hallucinations, confusion, speech disorder	1 hour	After taking zaleplon	Related
30710- 0007	20	F	Zaleplon 10 mg	Hallucinations	3 min	After taking zaleplon	Possibly related
30801- 0033	76	F	Zaleplon 10 mg	Hallucinations	3 hours	Unknown	Probably related
20419- 0119	30	F	Zaleplon 20 mg	Hallucinations	15 min	Unknown	Possibly related
20429- 0013	21	F	Zaleplon 20 mg	Hallucinations, confusion, depression**	Less than 30 min	After taking zaleplon	Probably related
30325- 0271	42	F	Zaleplon 20 mg	Hallucinations, tremor, amnesia, muscle twitching vertigo, visual disturbances**	Persisted"	Unknown	Remotely related
30738- 0014	25	F	Zaleplon 20 mg	Hallucinations	20 min	Immediately after taking drug	Definitely related
31230- 0002	24	F	Zaleplon 20 mg	Hallucinations	Not known	20 minutes after taking drug	Possibly related
20208- 1104	24	M	Zaleplon 60 mg	Hallucinations	< 1 hour	Also during placebo run- in	Not related
20208- 1110	44	F	Zaleplon 60 mg	Hallucinations	30 min	30 minutes after taking drug	Probably related
20209- 1125	60	F	Zaleplon 60 mg	Hallucinations	2 hours	After taking zaleplon	Probably related
30820- 0004	70	F	Placebo RO	Hallucinations (auditory)	12 days	Unknown	Possibly related
20423- 0126	24	M	Zolpidem 10 mg	Hallucinations	5 min	Unknown	Related
20209- 1128	25	M	Triazolam 0.25 mg	Hallucinations	< 1 hour	After taking triazolam	Possibly related
20333- 3103	51	M	Triazolam 0.25 mg	Hallucinations	90 min	Before getting up in AM	Possibly related

** Concomitant adverse events with halucinations

8.1.2.3 Misc. CNS relatadverse events reported as serious					
Patient Number	Age(y)	Sex	Dose at Onset	Adverse Event	Drug Relationship
20520- 0042	27	F	Zaleplon 5 mg	Nausea, dizziness, sweating	Possibly related
30870- 0002	66	F	Zaleplon 5 mg	Malaise	Possibly related
20515- 0026	42	F	Zaleplon 10 mg	Incoordination, speech disorder, confusion, abnormal gait	Probably related
20730- 1452	64	F	Zaleplon 10 mg	Confusion	Possibly related
30348- 0061	53	M	Zaleplon 10 mg	Hostility	Possibly related
30419- 0529	57	F	Zaleplon 10 mg	Depression, goiter, bundle branch block**	Possibly related
20429- 0011	29	M	Zaleplon 20 mg	Depression	Probably related
30105- 4071	39	M	Zaleplon 20 mg	Dizziness, accidental injury**	Possibly related
30609- 5331	73	F	Placebo	Facial paralysis	Not related
30708- 0005	49	M	Placebo	Hostility	Not related
30729- 0002	20	F	Placebo	Sleep disorder	Possibly related
30309- 0475	54	F	Zolpidem 10 mg	Ataxia, vertigo, dizziness	Definitely related
** Events which appear on additional tables.					

8.1.2.5 Patients with reports of chest pain/ angina in Group G phase II/III studies.						
Treatment/Patient #	**Age**	**Sex**	**Dose at Onset**	**Adverse Event**	**Comments**	**Investigator assessment**
Zaleplon						
30628- 5176	73	F	Zaleplon 5 mg	Chest pain, ventricular extrasystoles,** premature atrial contractions,** asthma	Patient reported palpitations and left-sided chest heaviness	Possibly related
30838- 0121	72	M	Zaleplon 5 mg	Angina pectoris, cyanosis, back pain	Myocardial infarction was ruled out.	Not related
30610- 5080	68	M	Zaleplon 10 mg	Chest pain, dyspnea, BUN increased	Patient diagnosed with stress related chest pain.	Possibly related
30610- 5326	72	F	Zaleplon 10 mg	Accidental injury,** angina pectoris, electrocardiogram abnormal**	Symptoms of angina were associated with abnormal electrocardiogram	Possibly related
30617- 5357	72	M	Zaleplon 10 mg	Chest pain	Pain occurred 48 hours after strenuous physical labor. Cardiac evaluation was normal.	Possibly related
30619- 5250	67	M	Zaleplon 10 mg	AV block,** angina pectoris, pacemaker insertion, palpitations	Angina was associated with abnormal electrocardiogram.	Not related
30725- 0026	50	F	Zaleplon 10 mg	Chest pain, tachycardia,** dyspnea	Diagnosed as dyspepsia.	Possibly related
30709- 0003	39	F	Zaleplon 20 mg	Chest pain	Patient reported sharp pain upon awakening that radiated to back and right shoulder	Related
Placebo						
30834- 0096	72	M	Placebo	Angina pectoris, tachycardia,** dizziness	Myocardial infarction was ruled out.	Possibly related
30829- 0355	91	M	Placebo run- out	Chest pain	Patient had a history of myocardial infarction.	Not related

Table 8.1.3.1.1 Number (%) of patients who discontinued by primary reason: group D (placebo controlled, parallel group studies)

	Zal <5 mg	Zal 5 mg	Zal 10 mg	Zal 20 mg	All Zal	All Comp	Placebo	
Reason	(n = 28)	(n = 609)	(n = 1132)	(n = 300)	(n = 2069)	(n = 413)	(n = 744)	p- value [a]
Any Reason	1 (3.6)	56 (9.2)	76 (6.7)	33 (11.0)	166 (8.0)	43 (10.4)	56 (7.5)	0.0991
Safety- Related Reasons								
Adverse reaction	1 (3.6)	16 (2.6)	24 (2.1)	12 (4.0)	53 (2.6)	16 (3.9)	15 (2.0)	0.3509
Other medical event	--	2 (0.3)	1 (0.1)	--	3 (0.1)	--	4 (0.5)	0.3470
Lack of Efficacy								
Unsatisfactory response	--	13 (2.1)	17 (1.5)	7 (2.3)	37 (1.8)	9 (2.2)	16 (2.2)	0.9055
Other								
Failed to return	--	3 (0.5)	7 (0.6)	1 (0.3)	11 (0.5)	2 (0.5)	4 (0.5)	0.9989
Event unrelated to	--	--	--	1 (0.3)	1 (< 0.1)	--	--	0.1209
therapy								
Patient/ subject request	--	7 (1.1)	12 (1.1)	4 (1.3)	23 (1.1)	5 (1.2)	10 (1.3)	0.9971
Protocol violation	--	12 (2.0)	12 (1.1)	3 (1.0)	27 (1.3)	10 (2.4)	5 (0.7)	0.2216
Other non- medical	--	2 (0.3)	3 (0.3)	1 (0.3)	6 (0.3)	--	2 (0.3)	0.9866
event								
Lack of compliance	--	--	--	3 (1.0)	3 (0.1)	1 (0.2)	--	0.0001
Non- compliance	--	1 (0.2)	--	1 (0.3)	2 (0.1)	--	--	0.5951
a: Comparison among all treatment groups								

Table 8.1.3.1.2 Number (%) of patients who discontinued by primary reason: group F (open label, long term, extension studies)	
	All Zaleplon
Reason	(n = 1088)
Any Reason	482 (44.3)
Safety- Related Reasons	
Adverse reaction	94 (8.6)
Other non- medical event	26 (2.4)
Lack of Efficacy	
Unsatisfactory response	163 (15.0)
Other	
Failed to return	35 (3.2)
Patient/ subject request	110 (10.1)
Protocol violation	36 (3.3)
Other medical event	12 (1.1)
Investigator choice	3 (0.3)
Lack of compliance	3 (0.3)

APPEARS THIS WAY ON ORIGINAL

Table 8.1.4.3.2 Withdrawal emergent adverse events reported by > 1% of aptients in any zaleplon treatment group in the placebo controlled, parallel, double blind pooled study population (group D): number (% patients).

	Zaleplon						
Body System	5 mg	10 mg	5 or 10 mg	20 mg	All a	Comparators	Placebo
Study Event	(n = 609)	(n = 1132)	(n = 1741)	(n = 300)	(n = 2069)	(n = 413)	(n = 744)
Any adverse experience (1 or more)	146 (24)	281 (25)	427 (25)	56 (19)	488 (24)	91 (22)	169 (23)
Body As A Whole							
Abdominal pain	7 (1)	8 (< 1)	15 (< 1)	1 (< 1)	16 (< 1)	2 (< 1)	7 (< 1)
Back pain	4 (< 1)	12 (1)	16 (< 1)	1 (< 1)	17 (< 1)	4 (< 1)	7 (< 1)
Headache	26 (4)	57 (5)	83 (5)	14 (5)	97 (5)	22 (5)	29 (4)
Pain	6 (< 1)	19 (2)	25 (1)	3 (1)	28 (1)	3 (< 1)	11 (1)
Digestive System							
Nausea	4 (< 1)	7 (< 1)	11 (< 1)	3 (1)	14 (< 1)	6 (1)	8 (1)
Musculoskeletal System							
Myalgia	5 (< 1)	15 (1)	20 (1)	3 (1)	23 (1)	7 (2)	4 (< 1)
Nervous System							
Abnormal dreams	2 (< 1)	12 (1)	14 (< 1)	2 (< 1)	16 (< 1)	6 (1)	6 (< 1)
Dizziness	8 (1)	11 (< 1)	19 (1)	0	20 (< 1)	3 (< 1)	5 (< 1)
Nervousness	7 (1)	12 (1)	19 (1)	2 (< 1)	21 (1)	8 (2)	4 (< 1)
Respiratory System							
Pharyngitis	4 (< 1)	12 (1)	16 (< 1)	4 (1)	20 (< 1)	3 (< 1)	8 (1)
Rhinitis	7 (1)	11 (< 1)	18 (1)	3 (1)	21 (1)	6 (1)	4 (< 1)

a. This column contains 28 patients in group D who received < 5 mg zaleplon and who are not accounted for in other columns.

Table 8.1.5.3.1 Treatment Emergent Adverse Events Occurring at least 1% of the time in zaleplon treated patients and at rates greater than that of placebo patients.
These patients are pooled from the 28 day placebo controlled studies[a] (group C).

Body System	Zaleplon All Doses[b]	Placebo
Preferred Term	(n = 786)	(n = 277)
Body as a Whole		
Abdominal pain	6%	4%
Asthenia	6%	5%
Infection	5%	4%
Back pain	4%	3%
Fever	2%	1%
Malaise	1%	<1%
Cardiovascular System		
Migraine	1%	<1%
Palpitation	1%	0%
Digestive System		
Dry mouth	2%	1%
Anorexia	1%	<1%
Musculoskeletal System		
Myalgia	6%	4%
Nervous System		
Dizziness	8%	7%
Somnolence	5%	3%
Amnesia	3%	1%
Depression	3%	2%
Paresthesia	3%	1%
Tremor	2%	1%
Depersonalization	1%	<1%
Vertigo	1%	<1%
Respiratory System		
Sinusitis	2%	<1%
Skin and Appendages		
Herpes simplex	1%	<1%
Special Senses		
Eye pain	4%	3%
Hyperacusis	2%	<1%
Abnormal vision	1%	<1%
Urogenital System		
Dysmenorrhea	3%	2%
Urinary Tract Infection	1%	0%

a: Events reported by at least 1% of patients treated with zaleplon are included and are rounded to the nearest %. Events for which the incidence with zaleplon was at least 1% but equal to or less than that with placebo are not listed in the table, but included the following: accidental injury, flu syndrome, headache, neck pain, pain, diarrhea, dyspepsia, nausea, vomiting, arthralgia, abnormal dreams, anxiety, hypertonia, nervousness, thinking abnormal, twitching, cough increased, pharyngitis, rhinitis, rash, parosmia, and taste perversion.
b: All doses of zaleplon combined (5 mg = 239 patients; 10 mg = 274; 20 mg = 273)

Table 8.1.6.3.2.1 PCS criteria for laboratory analytes	
Test	Criteria
Hemoglobin	Decrease of ≥20 g/ L
Hematocrit	Decrease of ≥0.05
WBC count	Increase or decrease of 2 x 10^9/L and ONR
Platelet count	Increase≥20% above baseline value and abnormally high, or decrease of ≥20% below baseline value and abnormally low
Basophils	Any non- baseline value of > 0.150 x 10^9 L
Lymphocytes	Any non- baseline value of > 4 x 10^9 /L or <1.5 x 10^9 /L
Monocytes	Any non- baseline value of > 0.95 x 10^9 /L or < 0.2 x 10^9 /L
Neutrophils	< 1.5 x 10^9 /L
Eosinophils	> 0.5 x 10^9 /L or > 5% of WBC
Sodium	Increase or decrease of ≥5 mmol/ L and ONR
Potassium	Increase or decrease of ≥0.5 mmol/ L and ONR
Calcium	Increase or decrease of ≥0.5 mmol/ L and ONR
Chloride	Increase or decrease of ≥5 mmol/ L and ONR
BUN/ urea	≥1.5 x UNL
Creatinine	≥1.5 x ULN
Total bilirubin	≥1.5 x ULN
ALT/ SGPT	≥1.5 x ULN
AST/ SGOT	≥3 x ULN
Alkaline phosphatase	≥3 x ULN
Cholesterol	Increase of ≥1.3 mmol/ L and ONR
Glucose	≥10 mmol/ L or anything < 2.78 mmol/ L
Uric acid	Increase of ≥178 mmol/ L and ONR
Total protein	Change of ≥10 g/ L and ONR
Albumin	Decrease of ≥ 10 g/ L and ONR
Urinalysis	
Protein/ albumin	Positive or anything not negative
Glucose/ sugar	Positive or anything not negative
Hemoglobin/ blood	Positive or anything not negative

Table 8.1.6.3.2.2 Number (%) patients* with clinical laboratory values that exceeded PCS criteria (group D pool)

Test parameter	Zaleplon <5 mg (n = 28)	Zaleplon 5 mg (n = 609)	Zaleplon 10 mg (n = 1132)	Zaleplon 20 mg (n = 300)	All Zaleplon (n = 2069)	All CMP (n = 413)	Placebo (n = 744)
Basophils, absolute	1 / 23 (4.3)	5 / 578 (< 1.0)	10 / 1090 (< 1.0)	6 / 282 (2.1)	22 / 1973 (1.1)	4 / 396 (1.0)	9 / 707 (1.3)
BUN	--	2 / 307 (< 1.0)	2 / 782 (< 1.0)	--	4 / 1205 (< 1.0)	2 / 253 (< 1.0)	--
Bili, Total	2 / 28 (7.1)	1 / 583 (< 1.0)	13 / 1103 (1.2)	2 / 290 (< 1.0)	18 / 2004 (< 1.0)	1 / 397 (< 1.0)	3 / 716 (< 1.0)
Ca (-)	--	--	1 / 780 (< 1.0)	--	1 / 1079 (< 1.0)	--	--
Chol	--	--	1 / 472 (< 1.0)	--	1 / 473 (< 1.0)	--	1 / 146 (< 1.0)
Cl (+)	--	--	1 / 617 (< 1.0)	--	1 / 754 (< 1.0)	--	1 / 288 (< 1.0)
Cl (-)	--	1 / 137 (< 1.0)	--	--	1 / 754 (< 1.0)	--	2 / 288 (< 1.0)
Creatinine	--	--	3 / 1103 (< 1.0)	1 / 290 (< 1.0)	4 / 2005 (< 1.0)	--	--
Eosinophils, absolute	3 / 23 (13.0)	11 / 578 (1.9)	19 / 1093 (1.7)	6 / 284 (2.1)	39 / 1978 (2.0)	7 / 396 (1.8)	16 / 710 (2.3)
Eos	5 / 23 (21.7)	31 / 578 (5.4)	66 / 1095 (6.0)	28 / 284 (9.9)	130 / 1980 (6.6)	33 / 396 (8.3)	52 / 710 (7.3)
Gluc (+)	--	13 / 585 (2.2)	14 / 1103 (1.3)	1 / 290 (< 1.0)	28 / 2006 (1.4)	11 / 397 (2.8)	9 / 716 (1.3)
Gluc (-)	--	1 / 585 (< 1.0)	2 / 1103 (< 1.0)	2 / 290 (< 1.0)	5 / 2006 (< 1.0)	1 / 397 (< 1.0)	3 / 716 (< 1.0)
Hct	--	24 / 582 (4.1)	52 / 1100 (4.7)	10 / 288 (3.5)	86 / 1998 (4.3)	18 / 396 (4.5)	27 / 714 (3.8)
Hgb	--	6 / 584 (1.0)	17 / 1100 (1.5)	4 / 289 (1.4)	27 / 2001 (1.3)	5 / 396 (1.3)	8 / 716 (1.1)
K (+)	--	4 / 299 (1.3)	2 / 779 (< 1.0)	--	6 / 1078 (< 1.0)	1 / 111 (< 1.0)	5 / 390 (1.3)
K (-)	--	1 / 299 (< 1.0)	5 / 779 (< 1.0)	--	6 / 1078 (< 1.0)	1 / 111 (< 1.0)	2 / 390 (< 1.0)
Lymphocytes, absolute (+)	1 / 23 (4.3)	8 / 578 (1.4)	21 / 1093 (1.9)	2 / 285 (< 1.0)	32 / 1979 (1.6)	5 / 396 (1.3)	10 / 710 (1.4)
Lymphocytes, absolute (-)	5 / 23 (21.7)	168 / 578 (29.1)	277 / 1093 (25.3)	63 / 285 (22.1)	513 / 1979 (25.9)	89 / 396 (22.5)	194 / 710 (27.3)
Monocytes, absolute (+)	1 / 23 (4.3)	7 / 578 (1.2)	9 / 1093 (< 1.0)	1 / 285 (< 1.0)	18 / 1979 (< 1.0)	3 / 396 (< 1.0)	4 / 710 (< 1.0)
Monocytes, absolute (-)	3 / 23 (13.0)	14 / 578 (2.4)	21 / 1093 (1.9)	18 / 285 (6.3)	56 / 1979 (2.8)	15 / 396 (3.8)	16 / 710 (2.3)
Neutrophils, absolute	2 / 23 (8.7)	10 / 578 (1.7)	15 / 1092 (1.4)	6 / 284 (2.1)	33 / 1977 (1.7)	12 / 394 (3.0)	12 / 708 (1.7)
Na (+)	--	5 / 299 (1.7)	6 / 779 (< 1.0)	--	11 / 1078 (1.0)	--	8 / 390 (2.1)
Na (-)	--	7 / 299 (2.3)	11 / 779 (1.4)	--	18 / 1078 (1.7)	7 / 111 (6.3)	10 / 390 (2.6)
Plt (+)	--	8 / 582 (1.4)	4 / 1099 (< 1.0)	4 / 289 (1.4)	16 / 1998 (< 1.0)	5 / 394 (1.3)	6 / 714 (< 1.0)
Plt (-)	--	--	2 / 1099 (< 1.0)	--	2 / 1998 (< 1.0)	--	3 / 714 (< 1.0)
Prot, Total (+)	--	1 / 580 (< 1.0)	2 / 1099 (< 1.0)	--	3 / 1989 (< 1.0)	--	1 / 712 (< 1.0)
Prot, Total (-)	1 / 24 (4.2)	--	2 / 1099 (< 1.0)	1 / 286 (< 1.0)	4 / 1989 (< 1.0)	1 / 396 (< 1.0)	5 / 712 (< 1.0)
AST	--	2 / 583 (< 1.0)	1 / 1103 (< 1.0)	--	3 / 2004 (< 1.0)	1 / 397 (< 1.0)	1 / 715 (< 1.0)
ALT	--	1 / 584 (< 1.0)	2 / 1103 (< 1.0)	--	3 / 2005 (< 1.0)	--	3 / 714 (< 1.0)
Ur Blood	1 / 1 (100.0)	50 / 307 (16.3)	107 / 781 (13.7)	26 / 117 (22.2)	184 / 1206 (15.3)	38 / 253 (15.0)	62 / 397 (15.6)
Ur Gluc	--	23 / 585 (3.9)	22 / 1100 (2.0)	5 / 290 (1.7)	50 / 2003 (2.5)	10 / 396 (2.5)	21 / 715 (2.9)
Ur Prot	1 / 28 (3.6)	42 / 585 (7.2)	82 / 1094 (7.5)	32 / 290 (11.0)	157 / 1997 (7.9)	33 / 396 (8.3)	57 / 712 (8.0)
Uric Acid	--	1 / 584 (< 1.0)	2 / 1103 (< 1.0)	--	3 / 2005 (< 1.0)	2 / 396 (< 1.0)	--
WBC (+)	4 / 28 (14.3)	13 / 584 (2.2)	20 / 1100 (1.8)	4 / 289 (1.4)	41 / 2001 (2.0)	7 / 396 (1.8)	13 / 716 (1.8)
WBC (-)	--	8 / 584 (1.4)	21 / 1100 (1.9)	4 / 289 (1.4)	33 / 2001 (1.6)	6 / 396 (1.5)	7 / 716 (1.0)

*The number of patients with potentially clinically important values for a particular laboratory test result is shown divided by the number of patients who had at least one result for that laboratory test.

Table 8.1.6.3.1.1 Statistically significant differences in mean laboratory values for patients in group D pool

Parameter	Period	Treatment	N	Baseline Mean	On Therapy Mean	Adjusted Mean	On Therapy Change	Significant Change	Significance Between (p)
(Units)									
Lymphocytes (L/ L) Post		Placebo	666	0.3208	0.3179	0.3151	-0.0029		b (0.044), d (0.003), g (0.020)
		≤5 mg Zaleplon	556	0.3153	0.3166	0.3174	0.0013		
		10 mg Zaleplon	1043	0.3120	0.3180	0.3211	0.0060	< 0.01	
		20 mg Zaleplon	270	0.3273	0.3282	0.3210	0.0009		
		Triazolam or Zolpidem	376	0.3158	0.3263	0.3268	0.0104	< 0.01	
Lymphocytes,	DB Week 1	Placebo	111	2.258	2.129	2.079	-0.129	< 0.01	c (0.019), f (0.003), j (0.005)
Absolute (10^9/L)		≤5 mg Zaleplon	100	2.098	1.975	2.034	-0.123	< 0.01	
		10 mg Zaleplon	122	2.225	2.141	2.113	-0.085		
		20 mg Zaleplon	58	2.154	2.206	2.226	0.052		
		Triazolam or Zolpidem	74	2.146	2.011	2.035	-0.135	< 0.01	
Monocytes	Post	Placebo	666	0.0679	0.0686	0.0685	0.0006		e (0.006), f(0.012), g (0.002)
(L/ L)		≤5 mg Zaleplon	555	0.0705	0.0714	0.0700	0.0009		
		10 mg Zaleplon	1043	0.0682	0.0679	0.0677	-0.0003		
		20 mg Zaleplon	269	0.0635	0.0648	0.0671	0.0013		
		Triazolam or Zolpidem	374	0.0659	0.0657	0.0667	-0.0002		
Monocytes,	Post	Placebo	666	0.440	0.431	0.432	-0.009		a (0.035), e (0.011), f (0.020), g (0.001)
absolute (10^9/L)		≤5 mg Zaleplon	555	0.456	0.454	0.447	-0.002		
		10 mg Zaleplon	1043	0.450	0.435	0.431	-0.015	< 0.001	

a= Placebo vs ≤5 mg Zaleplon
b = Placebo vs 10 mg Zaleplon
c = Placebo vs 20 mg Zaleplon
d = Placebo vs Triazolam or Zolpidem
e =≤5 mg Zaleplon vs 10 mg Zaleplon
f =≤5 mg Zaleplon vs 20 mg Zaleplon
g = ≤5 mg Zaleplon vs Triazolam or Zolpidem
h = 10 mg Zaleplon vs 20 mg Zaleplon
i = 10 mg Zaleplon vs Triazolam or Zolpidem
j = 20 mg Zaleplon vs Triazolam or Zolpidem

Table 8.1.6.3.1.1 Statistically significant differences in mean laboratory values for patients in group D pool

Parameter	Period	Treatment	N	Baseline Mean	On Therapy Mean	Adjusted Mean	On Therapy Change	Significant Change	Significance Between (p)
		20 mg Zaleplon	269	0.411	0.408	0.426	-0.003		
		Triazolam or Zolpidem	374	0.431	0.414	0.420	-0.017	< 0.01	
Basophils (L/ L)	Post	Placebo	662	0 0078	0.0082	0.0082	0.0004	< 0.05	b (0.038), c (0.002), f (0.042)
		≤5 mg Zaleplon	556	0 0078	0.0079	0.0079	0.0001		
		10 mg Zaleplon	1040	0.0077	0.0078	0.0078	0.0001		
		20 mg Zaleplon	266	0.0080	0.0075	0.0074	0.0006	< 0.05	
		Triazolam or Zolpidem	371	0.0078	0.0079	0.0079	0.0001		
Bilirubin, total	DB Week 2	Placebo	246	9.74	9.42	9.44	-0.32		b (0.008)
(mol/ L) m		≤5 mg Zaleplon	292	9 73	9.75	9.78	0.03		
		10 mg Zaleplon	312	9.87	10.15	10.08	0.28		
		20 mg Zaleplon	4	8 94	6.91	7.47	-2.03		
		Triazolam or Zolpidem	134	9.69	9.93	9.99	0.25		
	DB Week 4	Placebo	229	10.09	9.37	9.10	-0.71	< 0.01	a (0.022), c (0 004), d (0.001)
		≤5 mg Zaleplon	185	8.83	9.23	9.79	0.39		
		10 mg Zaleplon	223	10.35	9.95	9 50	-0.40		
		20 mg Zaleplon	202	9.46	9.80	9.94	0.34		
		Triazolam or Zolpidem	210	9.46	9.89	10.03	0.43	< 0.05	
	Post	Placebo	672	10.07	9.48	9.43	-0.59	< 0.001	b (< 0.001), d (0.002)
		≤5 mg Zaleplon	568	9.83	9.64	9.76	-0.19		

a= Placebo vs ≤5 mg Zaleplon
b = Placebo vs 10 mg Zaleplon
c = Placebo vs 20 mg Zaleplon
d = Placebo vs Triazolam or Zolpidem
e =≤5 mg Zaleplon vs 10 mg Zaleplon
f =≤5 mg Zaleplon vs 20 mg Zaleplon
g = ≤5 mg Zaleplon vs Triazolam or Zolpidem
h = 10 mg Zaleplon vs 20 mg Zaleplon
i = 10 mg Zaleplon vs Triazolam or Zolpidem
j = 20 mg Zaleplon vs Triazolam or Zolpidem

Table 8.1.6.3.1.1 Statistically significant differences in mean laboratory values for patients in group D pool

Parameter	Period	Treatment	N	Baseline Mean	On Therapy Mean	Adjusted Mean	On Therapy Change	Significant Change	Significance Between (p)
		10 mg Zaleplon	1056	10.15	10.09	9.98	-0.06		
		20 mg Zaleplon	271	10.12	9.84	9.76	-0.28		
		Triazolam or Zolpidem	372	9.65	9.79	10.04	0.14		
AST	DB Week 2	Placebo	248	20.7	21.1	21.4	0.4		a (0.029), g (0.004), i (0.028)
(units)		≤5 mg Zaleplon	294	21.1	20.6	20.6	-0.5		
		10 mg Zaleplon	313	21.4	21.1	20.9	-0.3		
		20 mg Zaleplon	4	17.8	16.8	19.3	-1.0		
		Triazolam or Zolpidem	135	21.1	21.8	21.8	0.7		
ALT	DB Week 4	Placebo	235	20.4	21.1	20.7	0.7		a (0.002), b (0.001), c (0.005), d (0.038)
(units)		≤5 mg Zaleplon	184	19.7	18.2	18.4	-1.4	< 0.05	
		10 mg Zaleplon	222	20.1	18.5	18.4	-1.6	< 0.001	
		20 mg Zaleplon	205	18.8	17.8	18.7	-1.0	< 0.05	
		Triazolam or Zolpidem	212	20.5	19.7	19.3	-0.8		
Sodium	Post	Placebo	368	139.2	139.1	138.8	-0.1		a (0.017), e (< 0.001), g (0.006)
(mmol/ L)		≤5 mg Zaleplon	278	139.4	139.7	139.3	0.3		
		10 mg Zaleplon	759	138.3	138.4	138.6	0.1		
		Triazolam or Zolpidem	106	137.9	138.0	138.5	0.2		

a= Placebo vs ≤5 mg Zaleplon
b = Placebo vs 10 mg Zaleplon
c = Placebo vs 20 mg Zaleplon
d = Placebo vs Triazolam or Zolpidem
e =≤5 mg Zaleplon vs 10 mg Zaleplon
f =≤5 mg Zaleplon vs 20 mg Zaleplon
g = ≤5 mg Zaleplon vs Triazolam or Zolpidem
h = 10 mg Zaleplon vs 20 mg Zaleplon
i = 10 mg Zaleplon vs Triazolam or Zolpidem
j = 20 mg Zaleplon vs Triazolam or Zolpidem

Table 8.1.7.3.1.1 Statistically significant changes in vital signs in group D patients

Parameter				Baseline	On Therapy	Adjusted	On Therapy	Significant	Significance Between
(Units)	Period	Treatment	N	Mean	Mean	Mean	Change	Change	Treatment Groups (p)
Respiration Rate (per minute)									d (0.002), g (0.013),
	DB Week 1	Placebo	291	16.3	16.3	16.2	0.0		i (0.001), j (0.021)
		≤ 5 mg zaleplon	167	16.1	16.3	16.4	0.2		
		10 mg zaleplon	604	16.2	16.2	16.2	0.0		
		20 mg zaleplon	136	16.1	16.3	16.4	0.2		
		Triazolam- zolpidem	105	16.4	17.2	17.1	0.8	< 0.01	
B. P., Diastolic, sitting (mm Hg)									
	DB Week 1	Placebo	514	77.4	76.0	75.5	-1.4	< 0.001	d (0.038), e (0.019),
									i (0.002)
		≤ 5 mg zaleplon	437	76.9	76.2	76.1	-0.7	< 0.05	
		10 mg zaleplon	878	76.4	74.8	75.1	-1.6	< 0.001	
		20 mg zaleplon	253	76.0	75.1	75.7	-1.0	< 0.05	
		Triazolam- zolpidem	326	77.0	76.7	76.5	-0.2		
Pulse, sitting (beats/ min)									
	Post	Placebo	697	71.7	71.4	71.4	-0.4		e (0.044), i (0.003),
									j (0.011)
		≤ 5 mg zaleplon	586	71.6	71.1	71.2	-0.4		
		10 mg zaleplon	1062	71.9	72.1	72.0	0.2		
		20 mg zaleplon	282	71.3	71.9	72.2	0.6		
		Triazolam- zolpidem	386	71.7	70.7	70.7	-1.0	< 0.05	

a= Placebo vs ≤ 5 mg zaleplon
b = Placebo vs 10 mg zaleplon
c = Placebo vs 20 mg zaleplon
d = Placebo vs triazolam- zolpidem
e = ≤ 5 mg zaleplon vs 10 mg zaleplon
f = ≤ 5 mg zaleplon vs 20 mg zaleplon
g = ≤ 5 mg zaleplon triazolam-zolpibem
h = 10 mg zaleplon vs 20 mg zaleplon
i = 10 mg zaleplon vs triazolam- zolpidem
j = 20 mg zaleplon vs triazolam- zolpidem

Table 8.1.7.3.2.2 Number of patients in the group D pool with change in vital signs of potential clinical significance.

Test Parameter	Zaleplon<5mg (n = 28)	Zaleplon 5 mg (n = 609)	Zaleplon 10 mg (n = 1132)	Zaleplon 20 mg (n = 300)	All Zaleplon (n = 2069)	All Comparators (n = 413)	Placebo (n = 744)
Resp. Rate (+)	1 / 28 (3.6)	2 / 179 (1.1)	6 / 693 (< 1.0)	1 / 174 (< 1.0)	10 / 1074 (< 1.0)	2 / 178 (1.1)	1 / 365 (< 1.0)
Resp. Rate (-)	–	–	1 / 693 (< 1.0)	–	1 / 1074 (< 1.0)	–	–
Sitting Diastol BP (+)	–	4 / 463 (< 1.0)	8 / 975 (< 1.0)	6 / 298 (2.0)	18 / 1764 (1.0)	7 / 410 (1.7)	6 / 597 (1.0)
Sitting Diastol BP (-)	2 / 28 (7.1)	7 / 463 (1.5)	21 / 975 (2.2)	8 / 298 (2.7)	38 / 1764 (2.2)	11 / 410 (2.7)	19 / 597 (3.2)
Sitting Pulse (+)	–	–	–	1 / 298 (< 1.0)	1 / 2051 (< 1.0)	–	–
Sitting Pulse (-)	–	3 / 603 (< 1.0)	4 / 1122 (< 1.0)	6 / 298 (2.0)	13 / 2051 (< 1.0)	4 / 410 (1.0)	7 / 741 (< 1.0)
Sitting Systol BP (+)	–	1 / 463 (< 1.0)	3 / 975 (< 1.0)	2 / 298 (< 1.0)	6 / 1764 (< 1.0)	1 / 410 (< 1.0)	4 / 597 (< 1.0)
Sitting Systol BP (-)	2 / 28 (7.1)	7 / 463 (1.5)	13 / 975 (1.3)	7 / 298 (2.3)	29 / 1764 (1.6)	14 / 410 (3.4)	12 / 597 (2.0)
Standing Diastol BP (+)	–	–	1 / 148 (< 1.0)	–	1 / 288 (< 1.0)	–	2 / 144 (1.4)
Standing Diastol BP (-)	–	–	1 / 148 (< 1.0)	–	1 / 288 (< 1.0)	–	2 / 144 (1.4)
Standing Systol BP (+)	–	1 / 140 (< 1.0)	2 / 148 (1.4)	–	3 / 288 (1.0)	–	3 / 144 (2.1)
Standing Systol BP (-)	–	1 / 140 (< 1.0)	1 / 148 (< 1.0)	–	2 / 288 (< 1.0)	–	1 / 144 (< 1.0)
Supine Diastol BP (+)	–	--	3 / 148 (2.0)	–	3 / 289 (1.0)	–	2 / 144 (1.4)
Supine Diastol BP (-)	–	--	1 / 148 (< 1.0)	–	1 / 289 (< 1.0)	–	1 / 144 (< 1.0)
Supine Systol BP (+)	–	–	3 / 148 (2.0)	–	3 / 289 (1.0)	–	5 / 144 (3.5)
Temperature (+)	–	–	1 / 881 (< 1.0)	–	1 / 1330 (< 1.0)	–	–
Temperature (-)	1 / 28 (3.6)	5 / 362 (1.4)	4 / 881 (< 1.0)	4 / 59 (6.8)	14 / 1330 (1.1)	3 / 175 (1.7)	3 / 493 (< 1.0)
Weight (+)	–	–	4 / 476 (< 1.0)	–	4 / 476 (< 1.0)	–	–
Weight (-)	–	–	1 / 476 (< 1.0)	–	1 / 476 (< 1.0)	–	1 / 151 (< 1.0)

a: The number of patients with potentially clinically important values for a particular vital sign result is shown divided by the number of patients who had at least one result for that vital sign measurement.