Supplement 1
ADRs by initial treatment status with suvorexant

	Initial status of suvorexant treatment			
	Group N	Group S	Group A	Group O
Number of patients	1946	703	536	63
Number of patients with adverse drug reactions	132	110	68	5
Number of adverse drug reaction events	157	137	76	7
Rate of occurrence	6.78%	15.65%	12.69%	7.94%
Type of adverse drug reactions N (%)				
Mental disorder	26 (1.34)	49 (6.97)	24 (4.48)	1 (1.59)
Abnormal dreams	1 (0.05)	2 (0.28)	3 (0.56)	1 (1.59)
Agitation	1 (0.05)	-	-	-
Delirium	-	-	2 (0.37)	-
Depression	1 (0.05)	-	-	-
Disorientation	-	1 (0.14)	-	-
Dissociative disorder	-	-	1 (0.19)	-
Hallucination	1 (0.05)	-	-	-
Hallucination, visual	1 (0.05)	1 (0.14)	-	-
Hypnagogic hallucination	1 (0.05)	-	-	-
Initial insomnia	2 (0.10)	5 (0.71)	2 (0.37)	-
Insomnia	6 (0.31)	30 (4.27)	4 (0.75)	-
Irritability	1 (0.05)	-	-	-
Middle insomnia	1 (0.05)	3 (0.43)	2 (0.37)	-
Nervousness	-	1 (0.14)	-	-
Nightmare	11 (0.57)	8 (1.14)	8 (1.49)	-
REM sleep abnormality	-	-	1 (0.19)	-
Sleep talking	-	-	1 (0.19)	-
Suicidal ideation	1 (0.05)	-	-	-
Nervous system disorders	94 (4.83)	48 (6.83)	39 (7.28)	4 (6.35)
Disturbance in attention	1 (0.05)	-	-	-
Dizziness	20 (1.03)	8 (1.14)	7 (1.31)	-
Dyslalia	-	1 (0.14)	-	-
Head discomfort	1 (0.05)	1 (0.14)	-	-
Headache	5 (0.26)	5 (0.71)	2 (0.37)	-
Hypersomnia	2 (0.10)	1 (0.14)	3 (0.56)	-
Paraesthesia	-	-	1 (0.19)	-
Sedation	2 (0.10)	-	2 (0.37)	-
Sleep paralysis	4 (0.21)	1 (0.14)	-	-
Sleep phase rhythm disturbance	-	1 (0.14)	-	-
Somnolence	59 (3.03)	33 (4.69)	21 (3.92)	4 (6.35)
Cognitive disorder	-	-	1 (0.19)	-
Restless legs syndrome	-	-	1 (0.19)	-
Poor quality sleep	3 (0.15)	-	1 (0.19)	-
Angiopathy	2 (0.10)	-	-	-
Hot flush	2 (0.10)	-	-	-
Respiratory, thoracic and mediastinal disorders	1 (0.05)	1 (0.14)	2 (0.37)	-
Cough	-	1 (0.14)	-	-
Dyspnoea	-	1 (0.14)	-	-
Pneumonia aspiration	-	-	1 (0.19)	-
Rhinitis allergic	1 (0.05)	-	-	-
Sleep apnoea syndrome	-	-	1 (0.19)	-
Gastrointestinal disorders	4 (0.21)	7 (1.00)	4 (0.75)	-
Abdominal discomfort	-	-	1 (0.19)	-

Diarrhea	-	3 (0.43)	-	-
Gastritis	1 (0.05)	-	-	-
Nausea	3 (0.15)	3 (0.43)	3 (0.56)	-
Salivary hypersecretion	-	1 (0.14)	-	-
Skin and subcutaneous tissue disorders	2 (0.10)	5 (0.71)	1 (0.19)	-
Cold sweat	-	1 (0.14)	-	-
Drug eruption	1 (0.05)	-	-	-
Eczema	-	1 (0.14)	-	-
Hyperhidrosis	1 (0.05)	-	-	-
Night sweats	-	1 (0.14)	-	-
Pruritus	-	2 (0.28)	-	-
Rash	-	1 (0.14)	1 (0.19)	-
Renal and urinary disorders	1 (0.05)	-	-	-
Pollakiuria	1 (0.05)	-	-	-
General disorders and administration site conditi	18 (0.92)	17 (2.42)	6 (1.12)	1 (1.59)
Asthenia	1 (0.05)	-	-	-
Discomfort	-	1 (0.14)	-	-
Face edema	1 (0.05)	-	-	-
Feeling abnormal	6 (0.31)	4 (0.57)	1 (0.19)	-
Feeling cold	-	-	1 (0.19)	-
Hangover	5 (0.26)	2 (0.28)	-	-
Malaise	6 (0.31)	7 (1.00)	3 (0.56)	1 (1.59)
Edema peripheral	-	2 (0.28)	-	-
Thirst	-	1 (0.14)	1 (0.19)	1 (1.59)
Investigation	-	1 (0.14)	-	-
Blood glucose increased	-	1 (0.14)	-	-
Injury, poisoning and procedural complications	2 (0.10)	1 (0.14)	-	-
Fall	2 (0.10)	-	-	-
Femoral neck fracture	1 (0.05)	-	-	-
Subdural hematoma	-	1 (0.14)	-	-
Traumatic intracranial hemorrhage	-	1 (0.14)	-	-

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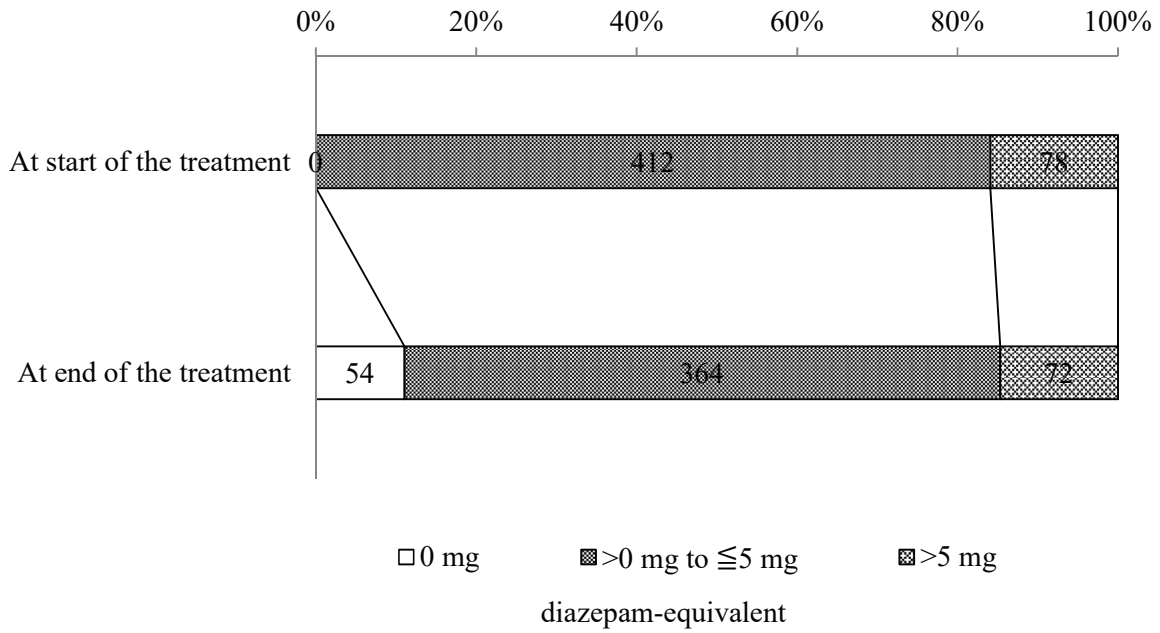
Supplement 2
Accumulative continuation/discontinuation status by initial treatment status

		Week 1 n (%)		Month 1 n (%)		Month 3 n (%)		Month 6 n (%)	
Overall (N=3248)	Continuing	3026	(93.2)	2433	(74.9)	1870	(57.6)	1577	(48.6)
	Completed treatment due to improvement	22	(0.7)	200	(6.2)	415	(12.8)	555	(17.1)
	Discontinued due to lack of efficacy	39	(1.2)	110	(3.4)	149	(4.6)	159	(4.9)
	Discontinued due to inadequate effect	43	(1.3)	187	(5.8)	305	(9.4)	354	(10.9)
	Discontinued due to adverse event	84	(2.6)	178	(5.5)	236	(7.3)	260	(8.0)
	Drop out due to no re-visits	22	(0.7)	98	(3.0)	194	(6.0)	237	(7.3)
	Others	12	(0.4)	42	(1.3)	79	(2.4)	106	(3.3)
Group N （N＝1946）	Continuing	1821	(93.6)	1439	(73.9)	1067	(54.8)	893	(45.9)
	Completed treatment due to improvement	19	(1.0)	171	(8.8)	341	(17.5)	434	(22.3)
	Discontinued due to lack of efficacy	23	(1.2)	66	(3.4)	87	(4.5)	94	(4.8)
	Discontinued due to inadequate effect	20	(1.0)	96	(4.9)	163	(8.4)	186	(9.6)
	Discontinued due to adverse event	37	(1.9)	75	(3.9)	103	(5.3)	108	(5.5)
	Drop out due to no re-visits	21	(1.1)	77	(4.0)	134	(6.9)	167	(8.6)
	Others	5	(0.3)	22	(1.1)	51	(2.6)	64	(3.3)
Group S （N＝703）	Continuing	634	(90.2)	513	(73.0)	421	(59.9)	354	(50.4)
	Completed treatment due to improvement	2	(0.3)	14	(2.0)	34	(4.8)	57	(8.1)
	Discontinued due to lack of efficacy	10	(1.4)	23	(3.3)	34	(4.8)	36	(5.1)
	Discontinued due to inadequate effect	18	(2.6)	60	(8.5)	86	(12.2)	105	(14.9)
	Discontinued due to adverse event	33	(4.7)	70	(10.0)	83	(11.8)	93	(13.2)
	Drop out due to no re-visits	0	(0.0)	13	(1.8)	32	(4.6)	38	(5.4)
	Others	6	(0.9)	10	(1.4)	13	(1.8)	20	(2.8)
Group A （N=536）	Continuing	508	(94.8)	428	(79.9)	334	(62.3)	291	(54.3)
	Completed treatment due to improvement	1	(0.2)	14	(2.6)	38	(7.1)	58	(10.8)
	Discontinued due to lack of efficacy	6	(1.1)	20	(3.7)	27	(5.0)	28	(5.2)
	Discontinued due to inadequate effect	5	(0.9)	25	(4.7)	50	(9.3)	56	(10.4)
	Discontinued due to adverse event	14	(2.6)	33	(6.2)	48	(9.0)	55	(10.3)
	Drop out due to no re-visits	1	(0.2)	6	(1.1)	24	(4.5)	27	(5.0)
	Others	12	(0.4)	42	(1.3)	79	(2.4)	106	(3.3)

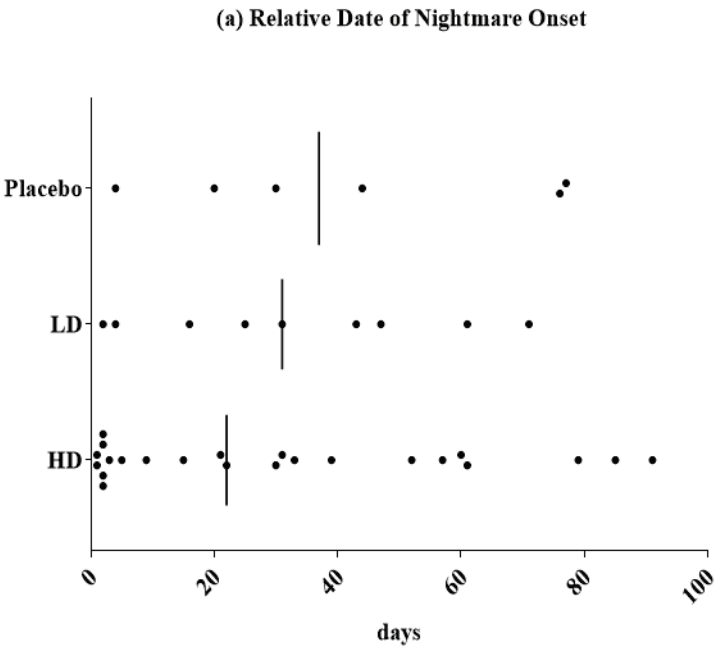
*Group O was not analyzed because of the small number. “Overall” includes patients in Groups N, S, A, and O.

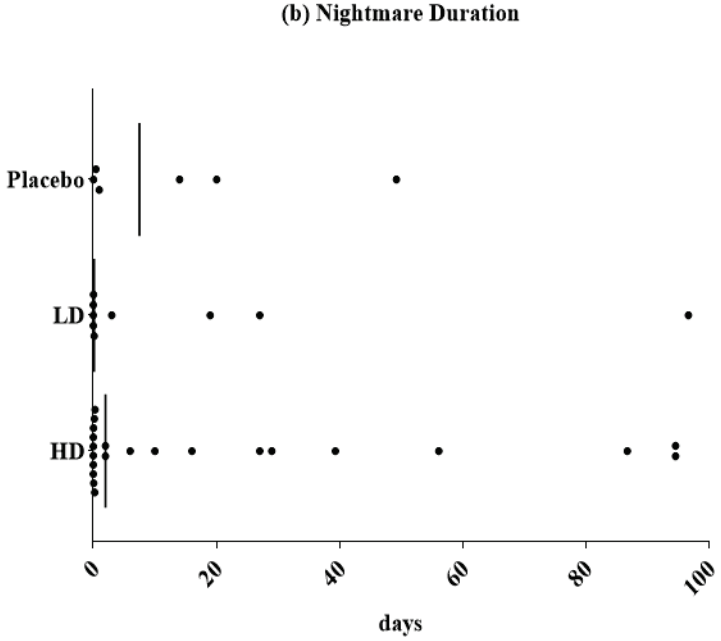
Supplement 3
Concomitant sleep medication classes in Group A at the initiation of treatment with suvorexant

Concomitant medications (hypnotics)		
Benzodiazepines	278	(51.9%)
Z-drugs	176	(32.8%)
Benzodiazepines and Z-drugs	39	(7.3%)
Melatonin receptor agonists	32	(6.0%)
Benzodiazepines and melatonin receptor agonists	5	(0.9%)
Z-drugs and melatonin receptor agonists	5	(0.9%)
Benzodiazepines, Z-drugs and melatonin receptor agonists	1	(0.2%)
Total	536	100.0%



Supplement 4
Dosing conditions of concomitant benzodiazepine/non-benzodiazepine in Group A at the initiation of treatment with suvorexant and end of the PMS. The dosing of BzRAs was categorized into following three diazepam-equivalent dose groups. 1) 0 mg, 2) >0 mg to ≤5 mg, 3) >5 mg, Data labels indicate the number of patients.





Supplement 5
Nightmare: relative date of the onset (a) and the duration (b) in combined phase 3 population 0-3 months (P028, P029, and P009). High dose (HD): suvorexant 40 mg for non-elderly (18 to <65 years) and 30 mg for elderly (≥65 years); low dose (LD): suvorexant 20 mg for non-elderly and 15 mg for elderly. Dots indicate a nightmare event and the bars indicate the median. One patient who had not been recovered in HD is not shown in the graph (b).