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Protocol Registration and Results System

ID: 99824 Safety Study of Sertindole Versus Risperidone Under Normal Conditions of Use NCT00856583

Protocol Registration and Results Preview

Close

Safety Study of Sertindole Versus Risperidone Under Normal Conditions of Use (SCoP)

This study has been completed.

Sponsor:	H. Lundbeck A/S
Collaborators:	
Information provided by:	H. Lundbeck A/S
ClinicalTrials.gov Identifier:	NCT00856583

Purpose

The purpose of the study is to determine whether there is an increased all-cause mortality in sertindole-treated patients in comparison to patients treated with a well-known antipsychotic (risperidone) when used under normal marketed conditions in the treatment of schizophrenia.

Condition	Intervention	Phase
Schizophrenia	Drug: Sertindole Drug: Risperidone	Phase 3

Study Type: Interventional
Study Design: Prevention, Parallel Assignment, Open Label, Randomized, Safety Study

Official Title: Sertindole Versus Risperidone Safety Outcome Study: a Randomised, Partially-blinded, Parallel-group, Active-controlled, Post-marketing Study

Further study details as provided by H. Lundbeck A/S:

Primary Outcome Measure:

- Number of Participants With All-cause Mortality [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]
  The analysis was based on all deaths from the Whole Randomised Treatment (WRT)+30 days period and the Only Randomised Treatment (ORT) period, respectively

- Second Primary Outcome: Number of Participants With Cardiac Events, Including Arrhythmias, Requiring Hospitalisation [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]
  Second primary endpoint: a serious adverse event where the patient was hospitalised and for which the Independent Safety Committee (ISC) classified the event as a cardiac event with documented arrhythmia. The analysis of this outcome was not performed due to low number of events. The presented analysis is a replacement analysis using all cardiac events, including arrhythmias, that required hospitalisation

Secondary Outcome Measures:

- Cause-specific Mortality: Number of Participants With Cardiac Deaths - ISC [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]

  The analysis was based on all deaths from the WRT+30 days period using the classification performed by the ISC. The ISC reviewed and classified those adverse events which resulted in death or hospitalisation or were possible suicide attempts and this review was blinded to exposure. The definition of cardiac death was intentionally wide; sudden or unexplained deaths were assumed to be cardiac if there was no non-cardiac explanation. To ensure consistent evaluation and classification, the ISC decided a priori to classify all instances of self harm as possible suicide.

- Cause-specific Mortality: Number of Participants With Completed Suicides - ISC [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]

  The analysis was based on all deaths from the WRT+30 days period using the classification performed by the ISC. The ISC reviewed and classified those adverse events which resulted in death or hospitalisation or were possible suicide attempts and this review was blinded to exposure. The definition of cardiac death was intentionally wide; sudden or unexplained deaths were assumed to be cardiac if there was no non-cardiac explanation. To ensure consistent evaluation and classification, the ISC decided a priori to classify all instances of self harm as possible suicide.

- Cause-specific Mortality: Number of Participants With Other Than Cardiac Deaths and Completed Suicides - ISC [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]

  The analysis was based on all deaths from the WRT+30 days period using the classification performed by the ISC. The ISC reviewed and classified those adverse events which resulted in death or hospitalisation or were possible suicide attempts and this review was blinded to exposure. The definition of cardiac death was intentionally wide; sudden or unexplained deaths were assumed to be cardiac if there was no non-cardiac explanation. To ensure consistent evaluation and classification, the ISC decided a priori to classify all instances of self harm as possible suicide.

- Cause-specific Mortality: Number of Participants With Cardiac Deaths - MedDRA [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]

  The analysis was based on all deaths from the WRT+30 days period using the classification based upon the Medical Dictionary for Regulatory Activities (MedDRA) terminology, that is, as reported by the investigator

- Cause-specific Mortality: Number of Participants With Completed Suicides - MedDRA [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]

  The analysis was based on all deaths from the WRT+30 days period using the classification based upon MedDRA terminology, that is, as reported by the investigator

- Cause-specific Mortality: Number of Participants With Other Than Cardiac Deaths and Completed Suicides - MedDRA [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]
  The analysis was based on all deaths from the WRT+30 days period using the classification based upon MedDRA terminology, that is, as reported by the investigator

- Number of Participants With Suicide Attempts (Fatal and Non-fatal) - ISC [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]
  The analysis was based on all suicides and suicide attempts from the WRT+30 days period using the classification performed by the ISC. The ISC reviewed and classified those adverse events which resulted in death or hospitalisation or were possible suicide attempts and this review was blinded to exposure. The definition of cardiac death was intentionally wide; sudden or unexplained deaths were assumed to be cardiac if there was no non-cardiac explanation. To ensure consistent evaluation and classification, the ISC decided a priori to classify all instances of self harm as possible suicide.

- Number of Participants With Suicide Attempts (Fatal and Non-fatal) - MedDRA [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]
  The analysis was based on all suicides and suicide attempts from the WRT+30 days period using the classification based upon MedDRA terminology, that is, as reported by the investigator

- Number of Participants With Hospitalisations, Excluding Hospitalisations Related to the Primary Psychiatric Disease [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]
  The analysis was based on time from start of study drug to first hospitalisation during the WRT+30 days period

- Number of Participants With Discontinuation of Treatment for Any Reason Other Than Study Closure [Time Frame: As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months] [Designated as safety issue: Yes]
  The analysis was based on time from start of study drug until stop of study drug for any reason other than sponsor closure of the study

Enrollment: 9809
Study Start Date: July 2002
Study Completion Date: February 2008
Primary Completion Date: February 2008

Arms	Assigned Interventions
Experimental: Sertindole Normally in the range of	Drug: Sertindole Sertindole was supplied as 4, 12, 16, and 20 mg tablets. The start and maintenance dosages as well as dose titration were set by the investigator, in accordance with the national Summary of Product Characteristics (SPC) for sertindole; in countries where sertindole was not marketed, the European

4 to 20 mg/day	Union (EU) SPC applied (all national and EU SPCs were essentially identical). Recommended dose range: 12 to 20 mg/day. The investigators were instructed to contact H. Lundbeck A/S if they deemed it necessary to increase the dose of sertindole to 24 mg/day, which was allowed in exceptional cases Other Names: • Serdolect
Active Comparator: Risperidone Normally in the range of 2 to 8 mg/day	Drug: Risperidone Risperidone was supplied as 1, 2, 3, and 4 mg tablets. The start and maintenance dosages as well as dose titration were set by the investigator, in accordance with the national SPC for risperidone. Recommended dose range: 2 to 8 mg/day Other Names: • Risperdal

The Committee for Medicinal Products for Human Use (CHMP) requested a post-marketing study to ascertain that the favourable benefit-risk profile and low mortality rates seen in the clinical studies with sertindole would not be offset by higher mortality rates when sertindole was used under more normal conditions of use. It was recognised that, in a clinical trial setting, strict patient selection and monitoring could lead to higher compliance in patient management and thereby to a lower mortality rate. Study 99824 was therefore designed in collaboration with the CHMP as an open-label, randomised study with minimum study management that focused on mortality and general patient safety. The duration of the treatment period was not fixed. No efficacy measures were included.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Inclusion Criteria:

- The patient has signed the Informed Consent Form or, if he/she is not able to sign it (according to the ICH GCP guidelines and the Declaration of Helsinki), the patient's legal representative has signed the Informed Consent Form
- The patient has been diagnosed with schizophrenia
- Based on the patient's clinical status, new or change of antipsychotic treatment is indicated
- The patient is at least 18 years of age
- The patient meets the criteria set out in the national SPCs for sertindole and risperidone. For those countries in which sertindole was not marketed, the EU SPC applied

Exclusion Criteria:

- The last treatment taken by the patient was sertindole or risperidone
- The patient has never previously received any antipsychotic drug therapy
- The patient has contraindications to treatment with either sertindole or risperidone
- In addition to sertindole/risperidone, treatment with another antipsychotic is indicated
- The patient is homeless
- The patient has previously been included in one of the two H. Lundbeck A/S post-marketing studies, 99823 or 99824
- The patient is, in the opinion of the investigator, unlikely to comply with the study protocol or unsuitable for any other reason

Contacts and Locations

Investigators

Study Director: Email contact via H. Lundbeck A/S LundbeckClinicalTrials@lundbeck.com

More Information

Results Publications:

Peuskens J, Tanghøj P, Mittoux A; Sertindole Cohort. The Sertindole Cohort Prospective (SCoP) study: rationale, design and methodology. Pharmacoepidemiol Drug Saf. 2008 May;17(5):425-33. doi: 10.1002/pds.1594.

Thomas SH, Drici MD, Hall GC, Crocq MA, Everitt B, Lader MH, Le Jeunne C, Naber D, Priori S, Sturkenboom M, Thibaut F, Peuskens J, Mittoux A, Tanghøj P, Toumi M, Moore ND, Mann RD. Safety of sertindole versus risperidone in schizophrenia: principal results of the sertindole cohort prospective study (SCoP). Acta Psychiatr Scand. 2010 Nov;122(5):345-55. doi: 10.1111/j.1600-0447.2010.01563.x.

Crocq MA, Naber D, Lader MH, Thibaut F, Drici M, Everitt B, Hall GC, Le Jeunne C, Mittoux A, Peuskens J, Priori S, Sturkenboom M, Thomas SH, Tanghøj P, Toumi M, Mann R, Moore ND. Suicide attempts in a prospective cohort of patients with schizophrenia treated with sertindole or risperidone. Eur Neuropsychopharmacol. 2010 Dec;20(12):829-38. doi: 10.1016/j.euroneuro.2010.09.001.

De Hert M, Mittoux A, He Y, Peuskens J. Metabolic parameters in the short- and long-term treatment of schizophrenia with sertindole or risperidone. Eur Arch Psychiatry Clin Neurosci. 2011 Jun;261(4):231-9. doi: 10.1007/s00406-010-0142-x. Epub 2010 Sep 5.

De Hert M, Mittoux A, He Y, Peuskens J. A head-to-head comparison of sertindole and risperidone on metabolic parameters. Schizophr Res. 2010 Nov;123(2-3):276-7. doi: 10.1016/j.schres.2010.07.030. Epub 2010 Aug 21.

Responsible Party: H. Lundbeck A/S (H. Lundbeck A/S)

Study ID Numbers: 99824
2004-000213-19 [EudraCT Number]

Health Authority: Austria: Agency for Health and Food Safety
Belgium: Federal Agency for Medicinal Products and Health Products
Bulgaria: Bulgarian Drug Agency
Croatia: Agency for Medicinal Product and Medical Devices
Czech Republic: State Institute for Drug Control
Denmark: Danish Medicines Agency
Estonia: The State Agency of Medicine
Finland: Finnish Medicines Agency
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Germany: Federal Institute for Drugs and Medical Devices
Greece: Ministry of Health and Welfare
Hong Kong: Department of Health
Hungary: National Institute of Pharmacy
India: Drugs Controller General of India
Italy: National Monitoring Centre for Clinical Trials - Ministry of Health
Latvia: State Agency of Medicines
Lithuania: State Medicine Control Agency - Ministry of Health
Luxembourg: Ministère de la Santé
Malaysia: Ministry of Health
Netherlands: Medicines Evaluation Board (MEB)
Norway: Norwegian Medicines Agency
Philippines: Bureau of Food and Drugs
Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
Portugal: National Pharmacy and Medicines Institute
Romania: National Medicines Agency

Russia: FSI Scientific Center of Expertise of Medical Application
Serbia and Montenegro: Agency for Drugs and Medicinal Devices
Singapore: Clinical Trials & Epidemiology Research Unit (CTERU)
Slovakia: State Institute for Drug Control
South Korea: Korea Food and Drug Administration (KFDA)
Spain: Spanish Agency of Medicines
Sweden: Medical Products Agency
Switzerland: Swissmedic
Taiwan: National Bureau of Controlled Drugs
Thailand: Food and Drug Administration
Turkey: Ministry of Health
Ukraine: Ministry of Health
United Kingdom: Medicines and Healthcare Products Regulatory Agency

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Study Results

Participant Flow

Recruitment Details	593 centres in 38 countries (Europe and Asia). First patient first visit: 11 July 2002. Last patient last visit: 22 February 2008.
Pre-Assignment Details	

Arm/Group Title	Sertindole	Risperidone	Total (Not public)
▼ Arm/Group Description	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day	
Period Title: **Overall Study**			
Started	4905 [1]	4904 [2]	9809
Completed	1768 [3]	2307 [4]	4075
Not Completed	3137	2597	5734
Reason Not Completed			
Lack of Efficacy	389	377	766
Serious Adverse Event (SAE)	99	65	164
Non-SAE: Mostly Asymptomatic ECGs	393	179	572
Non-compliance	305	262	567
Withdrawal by Subject	1092	919	2011
Physician Decision	59	82	141
Pregnancy	14	5	19
Other NOTE : "Other" is not sufficiently descriptive for "Other" Reason Not Completed. Please provide a more descriptive label.	92	104	196
Non-evaluable: Patient on Polytherapy	694	604	1298
(Not Public)	Not Completed = 3137 Total from all reasons = 3137	Not Completed = 2597 Total from all reasons = 2597	

[1] Patients treated
[2] Patients treated
[3] Patients who were still on study drug at the time of study closure
[4] Patients who were still on study drug at the time of study closure

Baseline Characteristics

Arm/Group Title ▼ Arm/Group Description	Sertindole Normally in the range of 4 to 20 mg/day	Risperidone Normally in the range of 2 to 8 mg/day	Total
Overall Number of Baseline Participants	4905	4904	**9809**
▼ Baseline Analysis Population Description [Not specified]			
Age, Continuous Mean (Standard Deviation) Units: years	38.4 (11.8)	38.3 (11.7)	38.3 (11.8)
Age, Customized Measure Type: Number Units: participants			
18 to 65 years	4806	4820	9626
> 65 years	99	84	183
Gender, Male/Female Measure Type: Number Units: participants			
Female	2195	2188	4383
Male	2710	2716	5426
Duration of schizophrenia Measure Type: Number Units: participants			
Unknown	125	87	212
< 5 years	1450	1468	2918
5 to 10 years	1254	1278	2532
> 10 years	2076	2071	4147
Reasons for prescription of study drug Measure Type: Number Units: participants			
Adverse drug reaction	1121	1072	2193
Lack of efficacy	2542	2580	5122
None or poor compliance	161	169	330
Patient's choice	992	979	1971
Other	89	104	193
Number of previous suicide			

attempts Measure Type: Number Units: participants			
Unknown	17	11	28
0 previous suicide attempts	4281	4288	8569
1 previous suicide attempt	378	377	755
2 previous suicide attempts	125	126	251
3 previous suicide attempts	52	53	105
4 previous suicide attempts	18	13	31
>= 5 previous suicide attempts	34	36	70
Time since last suicide attempt Measure Type: Number Units: participants			
No previous suicide attempt or unknown	4298	4301	8599
< 1 year	122	117	239
1 to 5 years	226	218	444
> 5 years	259	268	527

Outcome Measures

1. Primary Outcome

Title:	Number of Participants With All-cause Mortality
▼ Description:	The analysis was based on all deaths from the Whole Randomised Treatment (WRT)+30 days period and the Only Randomised Treatment (ORT) period, respectively
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data

▼ Analysis Population Description

The analysis population included all patients who took at least one dose of study drug.

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants		

Number of deaths (WRT+30 days)	64	61
Number of deaths (ORT)	40	44

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of the first primary outcome was the null hypothesis of an excess mortality in sertindole-treated patients compared to the mortality in risperidone-treated patients for the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	If the upper limit of the 90% confidence interval (CI) for the estimated all-cause mortality ratio was <1.5 (pre-specified), the null hypothesis was rejected. With this limit, 7,600 patient years of exposure (PYE) were required to ensure 80% power at the 5% significance level of rejecting the null hypothesis when

		assuming a mortality of 2 deaths per 100 PYE. As the actual mortality was only about half that anticipated, more exposure was necessary and the duration of the study increased markedly.
Statistical Test of Hypothesis	P-Value	0.05
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age, sex, time since last suicide attempt, last previous antipsychotic treatment (mono-/polytherapy), year since start of enrollment.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.117
	Confidence Interval	(2-Sided) 90% 0.831 to 1.500
	Estimation Comments	The hazard ratio is calculated as sertindole (numerator) versus risperidone (denominator).

▼ Statistical Analysis 2 ✔

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of the first primary outcome was the null hypothesis of an excess mortality in sertindole-treated patients compared to the mortality in risperidone-treated patients for the ORT period.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	If the upper limit of the 90% CI for the estimated all-cause mortality ratio was <1.5 (pre-specified), the null hypothesis was rejected. With this limit, 7,600 PYE were required to ensure 80% power at the 5% significance level of rejecting the null hypothesis when assuming a mortality of 2 deaths per 100 PYE. As the actual mortality was only about half that anticipated, more

		exposure was necessary and the duration of the study increased markedly.
Statistical Test of Hypothesis	P-Value	<0.05
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age, sex, time since last suicide attempt, last previous antipsychotic treatment (mono-/polytherapy), year since start of enrollment.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.980
	Confidence Interval	(2-Sided) 90% 0.684 to 1.405
	Estimation Comments	The hazard ratio is calculated as sertindole (numerator) versus risperidone (denominator).

2. Primary Outcome

Title:	Second Primary Outcome: Number of Participants With Cardiac Events, Including Arrhythmias, Requiring Hospitalisation
▼ Description:	Second primary endpoint: a serious adverse event where the patient was hospitalised and for which the Independent Safety Committee (ISC) classified the event as a cardiac event with documented arrhythmia. The analysis of this outcome was not performed due to low number of events. The presented analysis is a replacement analysis using all cardiac events, including arrhythmias, that required hospitalisation
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data 

▼ Analysis Population Description

The analysis population included all patients who took at least one dose of study drug.

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants	4905	4904

Analyzed		
Measure Type: Number Units: participants	10	6

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of time to 1st occurence of the secondary primary outcome (one patient in the risperidone group reported more than one occurrence of this event) was the null hypothesis of hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.29
	Comments	[Not specified]

	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age and sex.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.73
	Confidence Interval	(2-Sided) 95% 0.63 to 4.78
	Estimation Comments	[Not specified]

3. Secondary Outcome

Title:	Cause-specific Mortality: Number of Participants With Cardiac Deaths - ISC
▼ Description:	The analysis was based on all deaths from the WRT+30 days period using the classification performed by the ISC. The ISC reviewed and classified those adverse events which resulted in death or hospitalisation or were possible suicide attempts and this review was blinded to exposure. The definition of cardiac death was intentionally wide; sudden or unexplained deaths were assumed to be cardiac if there was no non-cardiac explanation. To ensure consistent evaluation and classification, the ISC decided a priori to classify all instances of self harm as possible suicide.
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data ✔

▼ Analysis Population Description

The analysis population included all patients who took at least one dose of study drug.

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	31	12

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of this secondary outcome was the null hypothesis of mortality hazard ratio equal to 1 for the sertindole-

		treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.0022
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted: age, sex, time since last suicide attempt, last previous antipsychotic treatment (mono-/polytherapy), region, year since start of enrollment
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	2.84
	Confidence Interval	(2-Sided) 95% 1.45 to 5.55
	Estimation Comments	[Not specified]

4. Secondary Outcome

Title:	Cause-specific Mortality: Number of Participants With Completed Suicides - ISC
▼ Description:	The analysis was based on all deaths from the WRT+30 days period using the classification performed by the ISC. The ISC reviewed and classified those adverse events which resulted in death or hospitalisation or were possible suicide attempts and this review was blinded to exposure. The definition of cardiac death was intentionally wide; sudden or unexplained deaths were assumed to be cardiac if there was no non-cardiac explanation. To ensure consistent evaluation and classification, the ISC decided a priori to classify all instances of self harm as possible suicide.
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Sertindole	Risperidone

▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	14	21

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of this secondary outcome was the null hypothesis of mortality hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.34
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]

	Comments	Adjusted for: age, sex, time since last suicide attempt, last previous antipsychotic treatment (mono-/polytherapy), year since start of enrollment.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.72
	Confidence Interval	(2-Sided) 95% 0.36 to 1.41
	Estimation Comments	[Not specified]

5. Secondary Outcome

Title:	Cause-specific Mortality: Number of Participants With Other Than Cardiac Deaths and Completed Suicides - ISC
▼ Description:	The analysis was based on all deaths from the WRT+30 days period using the classification performed by the ISC. The ISC reviewed and classified those adverse events which resulted in death or hospitalisation or were possible suicide attempts and this review was blinded to exposure. The definition of cardiac death was intentionally wide; sudden or unexplained deaths were assumed to be cardiac if there was no non-cardiac explanation. To ensure consistent evaluation and classification, the ISC decided a priori to classify all instances of self harm as possible suicide.
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	19	28

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis

		of this secondary outcome was the null hypothesis of mortality hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.26
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age, sex, last previous antipsychotic treatment (mono-/polytherapy), year since start of enrollment.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.715
	Confidence Interval	(2-Sided) 95% 0.40 to 1.28
	Estimation Comments	[Not specified]

6. Secondary Outcome

Title:	Cause-specific Mortality: Number of Participants With Cardiac Deaths - MedDRA
▼ Description:	The analysis was based on all deaths from the WRT+30 days period using the classification based upon the Medical Dictionary for Regulatory Activities (MedDRA) terminology, that is, as reported by the investigator
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data ✔

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants	4905	4904

Analyzed		
Measure Type: Number Units: participants	17	8

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of this secondary outcome was the null hypothesis of mortality hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.081
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age, sex, last previous antipsychotic treatment (mono-/polytherapy).
Method of	Estimation Parameter	Hazard Ratio (HR)

Estimation	Estimated Value	2.13
	Confidence Interval	(2-Sided) 95% 0.91 to 4.98
	Estimation Comments	[Not specified]

7. Secondary Outcome

Title:	Cause-specific Mortality: Number of Participants With Completed Suicides - MedDRA
▼ Description:	The analysis was based on all deaths from the WRT+30 days period using the classification based upon MedDRA terminology, that is, as reported by the investigator
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	13	21

▼ Statistical Analysis 1

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of this secondary outcome was the null hypothesis of mortality hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical	P-Value	0.24

Test of Hypothesis	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age, sex, time since last suicide attempt, last previous antipsychotic treatment (mono-/polytherapy), year since start of enrollment.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.66
	Confidence Interval	(2-Sided) 95% 0.33 to 1.32
	Estimation Comments	[Not specified]

8. Secondary Outcome

Title:	Cause-specific Mortality: Number of Participants With Other Than Cardiac Deaths and Completed Suicides - MedDRA
▼ Description:	The analysis was based on all deaths from the WRT+30 days period using the classification based upon MedDRA terminology, that is, as reported by the investigator
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data ✓

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	34	32

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of this secondary outcome was the

		null hypothesis of mortality hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.59
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age, sex, last previous antipsychotic treatment (mono-/polytherapy), year since start of enrollment.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.14
	Confidence Interval	(2-Sided) 95% 0.70 to 1.85
	Estimation Comments	[Not specified]

9. Secondary Outcome

Title:	Number of Participants With Suicide Attempts (Fatal and Non-fatal) - ISC
▼ Description:	The analysis was based on all suicides and suicide attempts from the WRT+30 days period using the classification performed by the ISC. The ISC reviewed and classified those adverse events which resulted in death or hospitalisation or were possible suicide attempts and this review was blinded to exposure. The definition of cardiac death was intentionally wide; sudden or unexplained deaths were assumed to be cardiac if there was no non-cardiac explanation. To ensure consistent evaluation and classification, the ISC decided a priori to classify all instances of self harm as possible suicide.
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data

▼ Analysis Population Description

The analysis population included all patients who took at least one dose of study drug.

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	68	76

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of time to 1st occurence of this secondary outcome was the null hypothesis of hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.65
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]

	Comments	Adjusted for: age, sex, duration of schizophrenia, time since last suicide attempt, year since start of enrollment.

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.93
	Confidence Interval	(2-Sided) 95% 0.66 to 1.29
	Estimation Comments	[Not specified]

10. Secondary Outcome

Title:	Number of Participants With Suicide Attempts (Fatal and Non-fatal) - MedDRA
▼ Description:	The analysis was based on all suicides and suicide attempts from the WRT+30 days period using the classification based upon MedDRA terminology, that is, as reported by the investigator
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data 

▼ Analysis Population Description

[Not specified]

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	43	65

▼ Statistical Analysis 1 

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of time to 1st occurence of this secondary outcome was the null hypothesis of hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.044
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age, sex, duration of schizophrenia, time since last suicide attempt, year since start of enrollment.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.67
	Confidence Interval	(2-Sided) 95% 0.45 to 0.99
	Estimation Comments	[Not specified]

11. Secondary Outcome

Title:	Number of Participants With Hospitalisations, Excluding Hospitalisations Related to the Primary Psychiatric Disease
▼ Description:	The analysis was based on time from start of study drug to first hospitalisation during the WRT+30 days period NOTE : Outcome Measure Description is shorter than the Outcome Measure Title.
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data

▼ Analysis Population Description
The analysis population included all patients who took at least one dose of study drug.

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	174	149

▼ Statistical Analysis 1 ✓

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of time to 1st occurence of this secondary outcome was the null hypothesis of hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.040
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted for: age, sex, time since last suicide attempt, last antipsychotic medication (a-/typicals/both), region, year since start of enrollment.
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.26
	Confidence Interval	(2-Sided) 95% 1.01 to 1.57
	Estimation Comments	[Not specified]

12. Secondary Outcome

Title:	Number of Participants With Discontinuation of Treatment for Any Reason Other Than Study Closure
▼ Description:	The analysis was based on time from start of study drug until stop of study drug for any reason other than sponsor closure of the study
Time Frame:	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months
Safety Issue?	Yes

▼ Outcome Measure Data ✓

▼ Analysis Population Description

The analysis population included all patients who took at least one dose of study drug.

Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description:	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day
Number of Participants Analyzed	4905	4904
Measure Type: Number Units: participants	3136	2597

▼ Statistical Analysis 1 ✔

Statistical Analysis Overview	Comparison Groups	Sertindole, Risperidone
	Comments	The basis for the statistical analysis of this secondary outcome was the null hypothesis of hazard ratio equal to 1 for the sertindole-treated patients versus risperidone-treated patients during the WRT+30 days period.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.0001
	Comments	[Not specified]
	Method	Other [Cox Proportional Hazard]
	Comments	Adjusted: disease duration, time since last suicide attempt, last antipsychotic medication (a-/typicals/both), region, year since start of enrollment.

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.35
	Confidence Interval	(2-Sided) 95% 1.28 to 1.43
	Estimation Comments	[Not specified]

Adverse Events

Time Frame	As study design allowed patients to continue study drug until the study was closed, many patients were followed for several years, with an overall median time period of approximately 14 months.	
Additional Description	Data on all serious adverse events and non-serious cardiac adverse events were collected.	
Source Vocabulary Name	MedDRA (10.1)	
Assessment Type	Non-systematic Assessment	
Arm/Group Title	Sertindole	Risperidone
▼ Arm/Group Description	Normally in the range of 4 to 20 mg/day	Normally in the range of 2 to 8 mg/day

▼ Serious Adverse Events

	Sertindole		Risperidone	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	266/4905 (5.42%)		217/4904 (4.42%)	
Blood and lymphatic system disorders				
Anaemia [A]	2/4905 (0.04%)	2	3/4904 (0.06%)	3
Blood disorder [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Leukopenia [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Normochromic normocytic anaemia [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Cardiac disorders				
Acute myocardial infarction [A]	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Angina unstable [A]	0/4905 (0%)	0	1/4904 (0.02%)	2
Arrhythmia [A]	3/4905 (0.06%)	3	0/4904 (0%)	0
Atrial flutter [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Cardiac arrest [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Cardiac failure [A]	1/4905 (0.02%)	1	2/4904 (0.04%)	2
Cardiac failure acute [A]	4/4905 (0.08%)	4	1/4904 (0.02%)	1
Cardiac failure congestive [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Cardio-respiratory arrest [A]	3/4905 (0.06%)	3	2/4904 (0.04%)	2

Cardiomyopathy [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Cardiopulmonary failure [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Conduction disorder [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Myocardial infarction [A]	4/4905 (0.08%)	4	2/4904 (0.04%)	2
Myocardial ischaemia [A]	4/4905 (0.08%)	4	2/4904 (0.04%)	2
Palpitations [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Torsade de pointes [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Ventricular tachycardia [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Ear and labyrinth disorders				
Vertigo [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Endocrine disorders				
Hyperprolactinaemia [A]	3/4905 (0.06%)	3	3/4904 (0.06%)	3
Inappropriate antidiuretic hormone secretion [A]	0/4905 (0%)	0	2/4904 (0.04%)	2
Eye disorders				
Eyelid disorder [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Meibomianitis [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Retinal detachment [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Gastrointestinal disorders				
Abdominal discomfort [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Abdominal distension [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Abdominal pain [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Abdominal pain upper [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Abdominal strangulated hernia [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Acute abdomen [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Anal fistula [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Ascites [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Crohn's disease [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Duodenal ulcer [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Duodenitis [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Gastric haemorrhage [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Gastric polyps [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Gastric ulcer [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Gastric ulcer perforation [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Gastritis [A]	0/4905 (0%)	0	4/4904 (0.08%)	4
Gastrointestinal disorder [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Gastrointestinal haemorrhage [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Haematemesis [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Inguinal hernia [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Nausea [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Oesophageal stenosis [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Oesophageal ulcer [A]	1/4905 (0.02%)	1	0/4904 (0%)	0

Oesophageal ulcer haemorrhage [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Oesophagitis [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Pancreatic mass [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Pancreatitis acute [A]	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Peritonitis [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Rectal haemorrhage [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Rectal prolapse [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Vomiting [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
General disorders				
Asthenia [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Chest pain [A]	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Condition aggravated [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Death [A]	12/4905 (0.24%)	12	2/4904 (0.04%)	2
Drowning [A]	0/4905 (0%)	0	2/4904 (0.04%)	2
Generalised oedema [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Oedema peripheral [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Pyrexia [A]	1/4905 (0.02%)	1	3/4904 (0.06%)	3
Sudden death [A]	1/4905 (0.02%)	1	2/4904 (0.04%)	2
Hepatobiliary disorders				
Bile duct obstruction [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Cholecystitis [A]	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Cholelithiasis [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Hepatic cirrhosis [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Hepatocellular damage [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Immune system disorders				
Hypersensitivity [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Infections and infestations				
Amoebic dysentery [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Appendicitis [A]	3/4905 (0.06%)	3	3/4904 (0.06%)	3
Bronchitis [A]	3/4905 (0.06%)	3	0/4904 (0%)	0
Bronchopneumonia [A]	1/4905 (0.02%)	1	2/4904 (0.04%)	2
Dengue fever [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Gangrene [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Gastroenteritis [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Gastroenteritis bacterial [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Helicobacter infection [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Infection [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Infection in an immunocompromised host [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Laryngitis [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Liver abscess [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Meningitis tuberculous [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Obstructive chronic bronchitis	1/4905 (0.02%)	1	1/4904 (0.02%)	1

with acute exacerbation	A				
Osteomyelitis	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Parasitic gastroenteritis	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Pneumonia	A	7/4905 (0.14%)	9	7/4904 (0.14%)	7
Pneumonia chlamydial	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Postoperative wound infection	A	2/4905 (0.04%)	2	0/4904 (0%)	0
Pulmonary tuberculosis	A	4/4905 (0.08%)	4	2/4904 (0.04%)	2
Pyelonephritis acute	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Sepsis	A	1/4905 (0.02%)	1	2/4904 (0.04%)	2
Sinusitis	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Tuberculosis	A	0/4905 (0%)	0	2/4904 (0.04%)	3
Upper respiratory tract infection	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Urinary tract infection	A	1/4905 (0.02%)	1	3/4904 (0.06%)	3
Vaginal candidiasis	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Injury, poisoning and procedural complications					
Accidental exposure	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Accidental overdose	A	2/4905 (0.04%)	2	0/4904 (0%)	0
Acetabulum fracture	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Alcohol poisoning	A	0/4905 (0%)	0	2/4904 (0.04%)	2
Ankle fracture	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Burns third degree	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Carbon monoxide poisoning	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Contusion	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Drug toxicity	A	2/4905 (0.04%)	2	6/4904 (0.12%)	6
Excoriation	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Face injury	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Fall	A	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Femoral neck fracture	A	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Femur fracture	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Fracture	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Head injury	A	2/4905 (0.04%)	2	2/4904 (0.04%)	2
Heat stroke	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Hip fracture	A	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Intentional overdose	A	21/4905 (0.43%)	23	14/4904 (0.29%)	16
Joint injury	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Joint sprain	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Ligament injury	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Lower limb fracture	A	3/4905 (0.06%)	3	0/4904 (0%)	0
Medication error	A	1/4905 (0.02%)	2	0/4904 (0%)	0
Meniscus lesion	A	0/4905 (0%)	0	1/4904 (0.02%)	1

Multiple drug overdose intentional [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Multiple fractures [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Multiple injuries [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Overdose [A]	15/4905 (0.31%)	16	8/4904 (0.16%)	8
Pneumothorax traumatic [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Poisoning [A]	3/4905 (0.06%)	3	1/4904 (0.02%)	1
Road traffic accident [A]	4/4905 (0.08%)	4	3/4904 (0.06%)	3
Self mutilation [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Skull fracture [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Thermal burn [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Tibia fracture [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Traumatic brain injury [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Ulna fracture [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Upper limb fracture [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Investigations				
Alanine aminotransferase increased [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Aspartate aminotransferase increased [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Blood triglycerides increased [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Electrocardiogram QT prolonged [A]	17/4905 (0.35%)	18	0/4904 (0%)	0
Electrocardiogram repolarisation abnormality [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Hepatic enzyme increased [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Medical observation [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Weight increased [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Metabolism and nutrition disorders				
Diabetes mellitus [A]	4/4905 (0.08%)	4	1/4904 (0.02%)	1
Diabetes mellitus inadequate control [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Diabetic ketoacidosis [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Electrolyte imbalance [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Hyperglycaemia [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Hyperlipidaemia [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Hypoglycaemia [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Hypokalaemia [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Hyponatraemia [A]	0/4905 (0%)	0	2/4904 (0.04%)	2
Type 2 diabetis mellitus [A]	3/4905 (0.06%)	3	0/4904 (0%)	0
Musculoskeletal and connective tissue disorders				
Back pain [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	2

Intervertebral disc protrusion [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Muscle spasms [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Osteoarthritis [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Osteoporosis postmenopausal [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Pain in extremity [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Rhabdomyolysis [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Systemic lupus erythematosus [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Adrenal carcinoma [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Benign neoplasm of testis [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Brain neoplasm [A]	0/4905 (0%)	0	2/4904 (0.04%)	2
Breast cancer [A]	1/4905 (0.02%)	1	3/4904 (0.06%)	3
Colon cancer [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Gammopathy [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Gastric cancer [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Gastric neoplasm [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Hepatic neoplasm malignant [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Lung neoplasm malignant [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Metastases to central nervous system [A]	0/4905 (0%)	0	3/4904 (0.06%)	3
Non-Hodgkin's lymphoma [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Non-small cell lung cancer [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Ovarian cancer [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Scrotal cancer [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Squamous cell carcinoma of the cervix [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Uterine cancer [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Uterine leiomyoma [A]	3/4905 (0.06%)	3	0/4904 (0%)	0
Nervous system disorders				
Brain damage [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Cerebral haemorrhage [A]	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Cerebral infarction [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Cerebrovascular accident [A]	3/4905 (0.06%)	3	0/4904 (0%)	0
Cerebrovascular disorder [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Coma [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Convulsion [A]	4/4905 (0.08%)	4	5/4904 (0.1%)	6
Diabetic coma [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Dizziness [A]	3/4905 (0.06%)	3	1/4904 (0.02%)	1
Dyskinesia [A]	0/4905 (0%)	0	2/4904 (0.04%)	2

Epilepsy	A	5/4905 (0.1%)	5	3/4904 (0.06%)	3
Extrapyramidal disorder	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Grand mal convulsion	A	5/4905 (0.1%)	5	3/4904 (0.06%)	3
Headache	A	0/4905 (0%)	0	2/4904 (0.04%)	2
Hypoxic encephalopathy	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Loss of consciousness	A	2/4905 (0.04%)	2	2/4904 (0.04%)	2
Neuroleptic malignant syndrome	A	0/4905 (0%)	0	2/4904 (0.04%)	2
Status epilepticus	A	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Syncope	A	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Transient ischaemic attack	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Pregnancy, puerperium and perinatal conditions					
Blighted ovum	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Intra-uterine death	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Pregnancy	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Psychiatric disorders					
Completed suicide	A	13/4905 (0.27%)	13	21/4904 (0.43%)	21
Delirium	A	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Depression	A	2/4905 (0.04%)	2	3/4904 (0.06%)	3
Depressive symptom	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Drug abuse	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Intentional self-injury	A	3/4905 (0.06%)	3	3/4904 (0.06%)	3
Mania	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Psychotic disorder	A	2/4905 (0.04%)	2	0/4904 (0%)	0
Suicidal behaviour	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Suicidal ideation	A	7/4905 (0.14%)	7	4/4904 (0.08%)	4
Suicide attempt	A	29/4905 (0.59%)	30	45/4904 (0.92%)	49
Renal and urinary disorders					
Calculus urinary	A	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Renal colic	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Renal disorder	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Renal failure acute	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Urge incontinence	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Reproductive system and breast disorders					
Amenorrhoea	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Galactorrhoea	A	0/4905 (0%)	0	3/4904 (0.06%)	3
Haematosalpinx	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Menorrhagia	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Metrorrhagia	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Ovarian cyst	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Uterovaginal prolapse	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Respiratory, thoracic and					

mediastinal disorders				
Acute respiratory distress syndrome [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Asphyxia [A]	4/4905 (0.08%)	4	3/4904 (0.06%)	3
Aspiration [A]	3/4905 (0.06%)	3	0/4904 (0%)	0
Asthma [A]	3/4905 (0.06%)	5	0/4904 (0%)	0
Chronic obstructive pulmonary disease [A]	2/4905 (0.04%)	2	1/4904 (0.02%)	1
Cough [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Dyspnoea [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Emphysema [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Haemoptysis [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Hydrothorax [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Lung disorder [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Obstructive airways disorder [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Pneumonia aspiration [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Pulmonary embolism [A]	4/4905 (0.08%)	4	3/4904 (0.06%)	3
Pulmonary oedema [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Respiratory failure [A]	4/4905 (0.08%)	4	0/4904 (0%)	0
Status asthmaticus [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Skin and subcutaneous tissue disorders				
Rash pruritic [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Social circumstances				
Alcohol use [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Drug abuser [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Physical assault [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Social problem [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Treatment noncompliance [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Surgical and medical procedures				
Bunion operation [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Cholecystectomy [A]	1/4905 (0.02%)	1	2/4904 (0.04%)	2
Hernia repair [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Mastectomy [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Plastic surgery [A]	1/4905 (0.02%)	1	0/4904 (0%)	0
Tonsillectomy [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Varicose vein operation [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Vascular disorders				
Aortic aneurysm rupture [A]	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Deep vein thrombosis [A]	2/4905 (0.04%)	2	0/4904 (0%)	0
Haematoma [A]	0/4905 (0%)	0	1/4904 (0.02%)	1
Hypertension [A]	2/4905 (0.04%)	2	1/4904 (0.02%)	1
[A]				

Hypertensive crisis		1/4905 (0.02%)	1	0/4904 (0%)	0
Labile hypertension	A	1/4905 (0.02%)	1	0/4904 (0%)	0
Lymphoedema	A	0/4905 (0%)	0	1/4904 (0.02%)	1
Orthostatic hypotension	A	1/4905 (0.02%)	1	2/4904 (0.04%)	2
Phlebitis	A	1/4905 (0.02%)	1	1/4904 (0.02%)	1
Shock	A	1/4905 (0.02%)	1	0/4904 (0%)	0

Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (10.1)

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%			
	Sertindole		**Risperidone**	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	397/4905 (8.09%)		11/4904 (0.22%)	
Investigations				
Electrocardiogram QT prolonged [A]	397/4905 (8.09%)		11/4904 (0.22%)	

Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (10.1)

Limitations and Caveats

[Not Specified]

More Information

Certain Agreements

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

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

Publication of the results by the investigator will be subject to mutual agreement between the investigator and H. Lundbeck A/S.

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