Clinical trial results:
An International Phase 3, Randomized, Double-Blind, Active (Tolterodine)-Controlled Multicenter Extension Study to Evaluate the Long-Term Safety and Efficacy of Vibegron in Patients With Symptoms of Overactive Bladder

Summary

EudraCT number	2017-003294-33
Trial protocol	LV HU LT
Global end of trial date	25 July 2019

Results information

Result version number	v2 (current)
This version publication date	02 April 2021
First version publication date	27 January 2021
Version creation reason	• Correction of full data set Alignment with ClinicalTrials.gov record

Trial information

Trial identification

Sponsor protocol code	RVT-901-3004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03583372
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Urovant Sciences GmbH
Sponsor organisation address	Viaduktstrasse 8 4051, Basel, Switzerland,
Public contact	Clinical Trial Information Contact, Urovant Sciences GmbH, 41 (42) 2155999, info@urovant.com
Scientific contact	Clinical Trial Information Contact, Urovant Sciences GmbH, 41 (42) 2155999, info@urovant.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 June 2019
Global end of trial reached?	Yes
Global end of trial date	25 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was designed to evaluate the safety, tolerability, and efficacy of vibegron administered once daily in subjects with overactive bladder (OAB) for up to 52 weeks.

Protection of trial subjects:

Each investigator obtained approval of the study from a properly constituted Institutional Review Board (IRB), Research Ethics Board (REB), or Independent Ethics Committee (IEC) prior to study initiation. This study was conducted in compliance with Good Clinical Practice (GCP). Prior to participating in any study procedures, the study was discussed with each subject and/or with the subject's legally authorized representative, and written informed consent was obtained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 506
Worldwide total number of subjects	506
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	271
From 65 to 84 years	231
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 506 subjects with overactive bladder (OAB) who completed 12 weeks in Study RVT-901-3003 (NCT03492281) and were screened and randomized for this extension study, 505 received at least 1 dose of double-blind study drug (Safety Set Extension [SAF-Ext]: vibegron, N = 273; tolterodine, N = 232).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Assessor, Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	40 Weeks Vibegron 75 mg

Arm description:

Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of vibegron 75 mg once daily for 40 weeks. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Arm type	Experimental
Investigational medicinal product name	Vibegron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vibegron 75-mg tablet, administered as a single tablet, orally, once daily

Arm title	52 Weeks Vibegron 75 mg

Arm description:

Subjects who had been randomized in Study RVT-901-3003 to receive vibegron 75 milligrams (mg) were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to vibegron 75 mg were to receive 52 weeks total of vibegron. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Arm type	Experimental
Investigational medicinal product name	Vibegron
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vibegron 75-mg tablet, administered as a single tablet, orally, once daily

Arm title	40 Weeks Tolterodine ER 4 mg

Arm description:

Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of tolterodine extended release (ER) 4 mg once daily for 40 weeks. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Arm type	Experimental
Investigational medicinal product name	Tolterodine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Tolterodine ER 4-mg capsule, administered as a single capsule, orally, once daily

Arm title	52 Weeks Tolterodine ER 4 mg

Arm description:

Subjects who had been randomized in Study RVT-901-3003 to receive tolterodine ER 4 mg were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to tolterodine ER 4 mg were to receive 52 weeks total of tolterodine ER. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Arm type	Experimental
Investigational medicinal product name	Tolterodine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Tolterodine ER 4-mg capsule, administered as a single capsule, orally, once daily

Number of subjects in period 1[1]	40 Weeks Vibegron 75 mg	52 Weeks Vibegron 75 mg	40 Weeks Tolterodine ER 4 mg
Started	92	181	91
Completed	79	156	72
Not completed	13	25	19
Adverse event, serious fatal	1	-	-
Captured As Other In The Database	1	2	4
Subject Withdrawn Due To Sponsor	-	-	-
Consent withdrawn by subject	6	11	7
Physician decision	-	1	1
Adverse event, non-fatal	1	3	4
Lost to follow-up	4	6	3
Lack of efficacy	-	1	-
Protocol deviation	-	1	-

Number of subjects in period 1[1]	52 Weeks Tolterodine ER 4 mg
Started	141
Completed	123
Not completed	18
Adverse event, serious fatal	-

Captured As Other In The Database	1
Subject Withdrawn Due To Sponsor	1
Consent withdrawn by subject	8
Physician decision	1
Adverse event, non-fatal	4
Lost to follow-up	2
Lack of efficacy	1
Protocol deviation	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the 506 subjects with overactive bladder (OAB) who completed 12 weeks in Study RVT-901-3003 and were screened and randomized for this extension study, 505 received at least 1 dose of double-blind study drug (Safety Set Extension [SAF-Ext]). Baseline data are reported for members of the SAF-Ext.

Baseline characteristics

Reporting groups	
Reporting group title	40 Weeks Vibegron 75 mg
Reporting group description:	
Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of vibegron 75 mg once daily for 40 weeks. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.	
Reporting group title	52 Weeks Vibegron 75 mg
Reporting group description:	
Subjects who had been randomized in Study RVT-901-3003 to receive vibegron 75 milligrams (mg) were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to vibegron 75 mg were to receive 52 weeks total of vibegron. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.	
Reporting group title	40 Weeks Tolterodine ER 4 mg
Reporting group description:	
Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of tolterodine extended release (ER) 4 mg once daily for 40 weeks. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.	
Reporting group title	52 Weeks Tolterodine ER 4 mg
Reporting group description:	
Subjects who had been randomized in Study RVT-901-3003 to receive tolterodine ER 4 mg were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to tolterodine ER 4 mg were to receive 52 weeks total of tolterodine ER. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.	

Reporting group values	40 Weeks Vibegron 75 mg	52 Weeks Vibegron 75 mg	40 Weeks Tolterodine ER 4 mg
Number of subjects	92	181	91
Age categorical Units:			
< 40	9	11	5
≥ 40 to < 55	22	34	16
≥ 55 to < 65	25	43	27
≥ 65 to < 75	28	70	30
≥ 75	8	23	13
Age continuous Units: years			
arithmetic mean	58.8	62.1	62.1
standard deviation	± 13.69	± 12.39	± 12.14
Gender categorical Units: Subjects			
Female	73	140	70
Male	19	41	21
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	2	0	0
Asian	4	16	8
Black or African American	14	23	10
White	72	141	72
Other	0	1	1

Overactive Bladder (OAB) Type			
Urgency incontinence is the involuntary loss of urine accompanied by urgency (referred to as OAB Wet). In the absence of incontinence, OAB is referred to as OAB Dry.			
Units: Subjects			
Wet	71	146	70
Dry	21	35	21

Reporting group values	52 Weeks Tolterodine ER 4 mg	Total	
Number of subjects	141	505	
Age categorical Units:			
< 40	11	36	
≥ 40 to < 55	27	99	
≥ 55 to < 65	40	135	
≥ 65 to < 75	47	175	
≥ 75	16	60	
Age continuous Units: years			
arithmetic mean	60.6		
standard deviation	± 12.98	-	
Gender categorical Units: Subjects			
Female	112	395	
Male	29	110	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	2	
Asian	11	39	
Black or African American	26	73	
White	102	387	
Other	2	4	
Overactive Bladder (OAB) Type			
Urgency incontinence is the involuntary loss of urine accompanied by urgency (referred to as OAB Wet). In the absence of incontinence, OAB is referred to as OAB Dry.			
Units: Subjects			
Wet	108	395	
Dry	33	110	

End points

End points reporting groups

Reporting group title	40 Weeks Vibegron 75 mg

Reporting group description:

Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of vibegron 75 mg once daily for 40 weeks. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Reporting group title	52 Weeks Vibegron 75 mg

Reporting group description:

Subjects who had been randomized in Study RVT-901-3003 to receive vibegron 75 milligrams (mg) were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to vibegron 75 mg were to receive 52 weeks total of vibegron. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Reporting group title	40 Weeks Tolterodine ER 4 mg

Reporting group description:

Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of tolterodine extended release (ER) 4 mg once daily for 40 weeks. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Reporting group title	52 Weeks Tolterodine ER 4 mg

Reporting group description:

Subjects who had been randomized in Study RVT-901-3003 to receive tolterodine ER 4 mg were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to tolterodine ER 4 mg were to receive 52 weeks total of tolterodine ER. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Subject analysis set title	Overall vibegron 75 mg: SAF-Ext Population
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received 40 weeks and 52 weeks vibegron 75 milligrams (mg). Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of vibegron 75 mg once daily for 40 weeks in RVT-901-3004. Subjecs who received 52 weeks vibegron 75 mg were randomized to receive vibegron 75 mg in both studies. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex. The SAF-Ext is comprised of all subjects who received at least one dose of double-blind study treatment during RVT-901-3004.

Subject analysis set title	Overall tolterodine ER 4 mg: SAF-Ext Population
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects who received 40 weeks and 52 weeks tolterodine ER 4 mg. Subjects who had been randomized to the placebo group in RVT-901-3003 were randomized to receive blinded study treatment of tolterodine ER 4 mg once daily for 40 weeks in Study RVT-901-3004. Subjects who received 52 weeks tolterodine ER 4 mg were randomized to receive tolterodine ER 4 mg in both studies. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex. The SAF-Ext is comprised of all subjects who received at least one dose of double-blind study treatment during RVT-901-3004.

Subject analysis set title	40 Weeks Vibegron 75 mg: FAS-Ext Population
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of vibegron 75 mg once daily for 40 weeks. Full Analysis Set Extension (FAS-Ext) Population: all randomized OAB subjects who took at least 1 dose of double-blind study treatment during this extension study and had at least 1 subsequent evaluable change from Baseline (CFB) micturition measurement in this extension study.

Subject analysis set title	52 Weeks Vibegron 75 mg: FAS-Ext Population
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who had been randomized in Study RVT-901-3003 to receive vibegron 75 milligrams (mg) were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through

participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to vibegron 75 mg were to receive 52 weeks total of vibegron. FAS-Ext Population: all randomized OAB subjects who took at least 1 dose of double-blind study treatment during this extension study and had at least 1 subsequent evaluable CFB micturition measurement in this extension study.

Subject analysis set title	40 Weeks Tolterodine ER 4 mg: FAS-Ext Population
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of tolterodine extended release (ER) 4 mg once daily for 40 weeks. FAS-Ext Population: all randomized OAB subjects who took at least 1 dose of double-blind study treatment during this extension study and had at least 1 subsequent evaluable CFB micturition measurement in this extension study.

Subject analysis set title	52 Weeks Tolterodine ER 4 mg: FAS-Ext Population
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who had been randomized in Study RVT-901-3003 to receive tolterodine ER 4 mg were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to tolterodine ER 4 mg were to receive 52 weeks total of tolterodine ER. FAS-Ext Population: all randomized OAB subjects who took at least 1 dose of double-blind study treatment during this extension study and had at least 1 subsequent evaluable CFB micturition measurement in this extension study.

Subject analysis set title	40 Weeks Vibegron 75 mg: FAS-Ext-I Population
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of vibegron 75 mg once daily for 40 weeks. Full Analysis Set Extension for Incontinence (FAS-Ext-I) Population: all randomized OAB Wet subjects who were included in the FAS-I population in Study RVT-901-3003, who took at least 1 dose of double-blind study treatment in this extension study and had at least 1 subsequent evaluable CFB UUI measurement.

Subject analysis set title	52 Weeks Vibegron 75 mg: FAS-Ext-I Population
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who had been randomized in Study RVT-901-3003 to receive vibegron 75 milligrams (mg) were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to vibegron 75 mg were to receive 52 weeks total of vibegron. FAS-Ext-I Population: all randomized OAB Wet subjects who were included in the FAS-I population in Study RVT-901-3003, who took at least 1 dose of double-blind study treatment in this extension study and had at least 1 subsequent evaluable CFB UUI measurement.

Subject analysis set title	40 Weeks Tolterodine ER 4 mg: FAS-Ext-I Population
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of tolterodine extended release (ER) 4 mg once daily for 40 weeks. FAS-Ext-I Population: all randomized OAB Wet subjects who were included in the FAS-I population in Study RVT-901-3003, who took at least 1 dose of double-blind study treatment in this extension study and had at least 1 subsequent evaluable CFB UUI measurement.

Subject analysis set title	52 Weeks Tolterodine ER 4 mg: FAS-Ext-I Population
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who had been randomized in Study RVT-901-3003 to receive tolterodine ER 4 mg were to continue their same treatment once daily in a blinded fashion for 40 weeks. Thus, through participation in both Study RVT-901-3003 and this extension study, subjects originally randomized to tolterodine ER 4 mg were to receive 52 weeks total of tolterodine ER. FAS-Ext-I Population: all randomized OAB Wet subjects who were included in the FAS-I population in Study RVT-901-3003, who took at least 1 dose of double-blind study treatment in this extension study and had at least 1 subsequent evaluable CFB UUI measurement.

Primary: Number of Subjects with the Indicated Type of Treatment-emergent Adverse Event

End point title	Number of Subjects with the Indicated Type of Treatment-emergent Adverse Event[1]

End point description:

Adverse events were collected in subjects with overactive bladder (OAB) who previously completed treatment in Study RVT-901-3003. The treatment-emergent period was defined as the period of time from the first dose date of the active double-blind study treatment, whether in Study RVT-901-3003 or Study RVT-901-3004, through 28 days after the last dose of study treatment, or the date of initiation of another investigational agent or surgical intervention, whichever occurred first.

End point type	Primary

End point timeframe:

up to 56 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not conducted.

End point values	Overall vibegron 75 mg: SAF-Ext Population	Overall tolterodine ER 4 mg: SAF-Ext Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	273	232		
Units: subjects				
number (not applicable)				
Any TEAE	171	126		
Any study drug-related TEAE	59	46		
Any Grade ≥ 3 TEAE	10	8		
Any Grade ≥ 3 study drug-related TEAE	1	1		
Any treatment-emergent (TE) SAE	9	10		
Any study drug-related TE SAE	1	2		
Any TEAE leading to discontinuation of study drug	4	8		
Any TEAE of clinical interest	41	32		
Any study drug-related TEAE of clinical interest	14	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (CFB) at Week 52 in the Average Number of Micturitions per 24 Hours in all Overactive Bladder (OAB) Subjects

End point title	Change from Baseline (CFB) at Week 52 in the Average Number of Micturitions per 24 Hours in all Overactive Bladder (OAB) Subjects[2]

End point description:

A micturition/void is defined as “Urinated in Toilet” as indicated on the Patient Voiding Diary (PVD). The number of micturitions is defined as the number of times a subject voided in the toilet as indicated in the PVD. The average daily number of micturitions was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of micturitions that occurred on a Complete Diary Day (CDD) divided by the number of CDDs in the PVD. CFB was calculated as the post-BL value minus the BL value. "Per 24 hours” corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next

morning as recorded in the PVD). Covariates included in the mixed model for repeated measures (MMRM) were study visit, treatment, treatment by study visit interaction, Baseline, and the statistically significant terms in Study RVT-901-3003: OAB type (Wet versus Dry) and sex.

End point type	Secondary

End point timeframe:

Baseline; Week 52

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per protocol, only the 52-week treatment groups were included in the statistical analysis.

End point values	52 Weeks Vibegron 75 mg	52 Weeks Tolterodine ER 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152[3]	120[4]		
Units: micturitions per 24 hours				
least squares mean (standard error)	-2.4 (± 0.24)	-2.0 (± 0.26)		

Notes:

[3] - Full Analysis Set Extension (FAS-Ext) Population. Only subjects with evaluable data were analyzed.

[4] - FAS-Ext Population. Only subjects with evaluable data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: CFB at Week 52 in the Average Number of Urge Urinary Incontinence (UUI) Episodes per 24 Hours in OAB Wet Subjects

End point title	CFB at Week 52 in the Average Number of Urge Urinary Incontinence (UUI) Episodes per 24 Hours in OAB Wet Subjects[5]

End point description:

The number of UUI episodes is defined as the number of times a subject had checked "urge" as the main reason for the leakage in the PVD, regardless of whether more than one reason for leakage in addition to "urge" was checked. The average daily number of UUI episodes was calculated using the daily entries in the PVD (which was to be completed prior to each study visit) as the total number of UUI episodes that occurred on a CDD divided by the number of CDDs in the PVD. CFB was calculated as the post-BL value minus the BL value. "Per 24 hours" corresponds to one Diary Day (i.e., time between when subject got up for the day each morning and time subject got up for the day the next morning as recorded in the PVD). Covariates included in the MMRM were study visit, treatment, treatment by study visit interaction, Baseline, and the statistically significant terms in Study RVT-901-3003: sex. Only subjects with evaluable data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 52

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per protocol, only the 52-week treatment groups were included in the statistical analysis.

End point values	52 Weeks Vibegron 75 mg	52 Weeks Tolterodine ER 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[6]	91[7]		
Units: UUI episodes per 24 hours				
least squares mean (standard error)	-2.2 (± 0.15)	-1.7 (± 0.17)		

Notes:

[6] - Full Analysis Set Extension for Incontinence (FAS-Ext-I) Population

[7] - FAS-Ext-I Population

Statistical analyses

No statistical analyses for this end point

Secondary: CFB at Week 52 in the Average Number of Urgency Episodes (Need to Urinate Immediately) over 24 Hours in All OAB Subjects

End point title	CFB at Week 52 in the Average Number of Urgency Episodes (Need to Urinate Immediately) over 24 Hours in All OAB Subjects[8]

End point description:

The number of urgency episodes is defined as the number of times a subject had checked "need to urinate immediately" on a CDD divided by the number of CDDs in the PVD. CFB is calculated as the post-BL value minus the BL value. "Over 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). Covariates included in the MMRM were study visit, treatment, treatment by study visit interaction, Baseline, and the statistically significant terms in Study RVT-901-3003: OAB type (Wet versus Dry) and sex.

End point type	Secondary

End point timeframe:

Baseline; Week 52

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per protocol, only the 52-week treatment groups were included in the statistical analysis.

End point values	52 Weeks Vibegron 75 mg	52 Weeks Tolterodine ER 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152[9]	120[10]		
Units: urgency episodes over 24 hours				
least squares mean (standard error)	-3.4 (± 0.34)	-3.2 (± 0.37)		

Notes:

[9] - FAS-Ext Population. Only subjects with evaluable data were analyzed.

[10] - FAS-Ext Population. Only subjects with evaluable data were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: CFB at Week 52 in the Average Number of Total Urinary Incontinence Episodes over 24 Hours in OAB Wet Subjects

End point title	CFB at Week 52 in the Average Number of Total Urinary Incontinence Episodes over 24 Hours in OAB Wet Subjects[11]

End point description:

The number of total incontinence episodes is defined as the number of times a subject had checked the accidental urine leakage box in the PVD, including for reasons of "urge," "stress," or "other." CFB was calculated as the post-BL value minus the BL value. "Over 24 hours" corresponds to one Diary Day (i.e., time between when the subject got up for the day each morning and time the subject got up for the day the next morning as recorded in the PVD). Covariates included in the MMRM were study visit, treatment, treatment by study visit interaction, Baseline, and the statistically significant terms in Study RVT-901-

3003: sex. hr = hours.

End point type	Secondary

End point timeframe:

Baseline; Week 52

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Per protocol, only the 52-week treatment groups were included in the statistical analysis.

End point values	52 Weeks Vibegron 75 mg	52 Weeks Tolterodine ER 4 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[12]	91[13]		
Units: Urinary incontinence episodes over 24 hr				
least squares mean (standard error)	-2.5 (± 0.17)	-1.9 (± 0.19)		

Notes:

[12] - FAS-Ext-I Population. Only subjects with evaluable data were analyzed.

[13] - FAS-Ext-I Population. Only subjects with evaluable data were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 56 weeks

Adverse event reporting additional description:

Treatment-emergent adverse events were collected in members of the Safety Set Extension, comprised of all subjects who received at least one dose of double-blind study treatment during RVT-901-3004. Subjects were included in the treatment group corresponding to the study treatment they actually received for the analysis of safety data.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Overall vibegron 75 mg

Reporting group description:

Subjects who received 40 weeks and 52 weeks vibegron 75 milligrams (mg). Subjects who had been randomized to the placebo group in Study RVT-901-3003 were randomized to receive blinded study treatment of vibegron 75 mg once daily for 40 weeks in RVT-901-3004. Subjects who received 52 weeks vibegron 75 mg were randomized to receive vibegron 75 mg in both studies. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Reporting group title	Overall tolterodine ER 4 mg

Reporting group description:

Subjects who received 40 weeks and 52 weeks tolterodine ER 4 mg. Subjects who had been randomized to the placebo group in RVT-901-3003 were randomized to receive blinded study treatment of tolterodine ER 4 mg once daily for 40 weeks in Study RVT-901-3004. Subjects who received 52 weeks tolterodine ER 4 mg were randomized to receive tolterodine ER 4 mg in both studies. Subjects were stratified by Baseline Overactive Bladder Type (Wet versus Dry) and sex.

Serious adverse events	Overall vibegron 75 mg	Overall tolterodine ER 4 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 273 (3.30%)	10 / 232 (4.31%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 273 (0.37%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic stenosis			

subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 273 (0.37%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Pelvic fracture			
subjects affected / exposed	1 / 273 (0.37%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 273 (0.37%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis microscopic			
subjects affected / exposed	1 / 273 (0.37%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			

subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	0 / 273 (0.00%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 273 (0.37%)	1 / 232 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 273 (0.37%)	0 / 232 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Overall vibegron 75 mg	Overall tolterodine ER 4 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 273 (23.81%)	56 / 232 (24.14%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	24 / 273 (8.79%)	20 / 232 (8.62%)	
occurrences (all)	25	22	
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 273 (5.49%)	9 / 232 (3.88%)	
occurrences (all)	16	9	
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	5 / 273 (1.83%)	12 / 232 (5.17%)	
occurrences (all)	5	13	
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	13 / 273 (4.76%)	12 / 232 (5.17%)	
occurrences (all)	16	13	
Urinary tract infection			
subjects affected / exposed	18 / 273 (6.59%)	17 / 232 (7.33%)	
occurrences (all)	22	22	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported