



Clinical trial results:

Skeletal muscle-derived cell implantation in female patients with stress urinary incontinence: a multicenter, randomized, parallel-group, placebo-controlled clinical study

Summary

EudraCT number	2009-011797-15
Trial protocol	DE CZ BG PL
Global end of trial date	08 June 2011

Results information

Result version number	v1 (current)
This version publication date	02 April 2026
First version publication date	02 April 2026
Summary attachment (see zip file)	Implantation of Autologous Skeletal MuscleDerived Cells Combined with Electrical Stimulation in Patients with Stress Urinary Incontinence (2025-Rose_ICES13.pdf)

Trial information

Trial identification

Sponsor protocol code	IC-01-01-4-003
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Innovacell Biotechnologie AG
Sponsor organisation address	Mitterweg 24, Innsbruck, Austria, 6020
Public contact	Clinical Department Innovacell, Innovacell Biotechnologie AG, office@innovacell.com
Scientific contact	Clinical Department Innovacell, Innovacell Biotechnologie AG, office@innovacell.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	07 December 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2011
Global end of trial reached?	Yes
Global end of trial date	08 June 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to find the optimal cell count for functional regeneration of the urethral sphincter including safety evaluation stress urinary incontinence.

Protection of trial subjects:

The rights, safety, and well-being of trial participants are the primary considerations of this clinical trial and prevail over interests of science and society. The trial is conducted in full accordance with the International Conference of Harmonisation Good Clinical Practice (GCP), the Declaration of Helsinki, and applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 208
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Romania: 79
Country: Number of subjects enrolled	Czechia: 9
Worldwide total number of subjects	319
EEA total number of subjects	319

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)	222
From 65 to 84 years	97
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment of patients per site was not limited and was competitive across countries (4) and sites (32). Study recruitment started in June 2010 and was planned to last 8 months.

Pre-assignment

Screening details:

In total, 319 patients were screened and 263 of them were randomized in 4 treatment groups in a ratio 2:2:2:1. 227 were included in the safety data set and 217 patients were finally considered as the intention-to-treat (ITT) population.

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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Patients were randomized in an open manner to cell implantation or control groups and in a double-blind manner to: a) high or low cell count implantation, and b) to duloxetine or duloxetine-placebo treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Low Cell Count (CL1)

Arm description:

In this arm 0.2 x 10⁶ autologous skeletal muscle-derived cells (Low Cell Count) are implanted in female patients with stress urinary incontinence.

Arm type	Experimental
Investigational medicinal product name	Autologous skeletal muscle-derived cells
Investigational medicinal product code	
Other name	ICES13
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

The IMP containing either 0.2 x 10⁶ cells (Low Cell Count) or 10 x 10⁶ (High Cell Count) in cell transport medium and is stored in 3 cryovials (1ml/vial). Prior to implantation, the IMP is prepared and thawed by the addition of 1ml Ringer's lactate solution per vial. The single administration of the IMP is performed via a standardized ultrasound-directed transurethral injection.

Arm title	High cell count (CL2)
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Arm description:

In this arm 10 x 10⁶ autologous skeletal muscle-derived cells (Low Cell Count) are implanted in female patients with stress urinary incontinence.

Arm type	Experimental
Investigational medicinal product name	SMDC
Investigational medicinal product code	
Other name	ICES13
Pharmaceutical forms	Suspension for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

The IMP containing either 0.2 x 10⁶ cells (Low Cell Count) or 10 x 10⁶ (High Cell Count) in cell transport medium and is stored in 3 cryovials (1ml/vial). Prior to implantation, the IMP is prepared and thawed by the addition of 1ml Ringer's lactate solution per vial. The single administration of the IMP is performed via a standardized ultrasound-directed transurethral injection.

Arm title	Duloxetine-placebo (C1)
Arm description: Placebo (for Duloxetine arm)	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	M0938C/CPS1/10A
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: Capsules in identical shape and appearance to duloxetine, applied in the same manner as the active control.	
Arm title	Duloxetine (C2)
Arm description: Duloxetine with increasing concentration over the weeks of application was administered in this arm	
Arm type	Active comparator
Investigational medicinal product name	Duloxetine
Investigational medicinal product code	A702141/CPS1/10A
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 20mg/d duloxetine was applied for week one with an increasing dose of 20 mg/d to maximal 80 mg/d. The highest tolerated dosage was applied for 12 weeks. Further down titration of the medication was done for 2 weeks (50% reduction/ week).	

Number of subjects in period 1^[1]	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)
Started	64	56	72
Completed	61	56	68
Not completed	3	0	4
Lost to follow-up	3	-	4

Number of subjects in period 1^[1]	Duloxetine (C2)
Started	35
Completed	32
Not completed	3
Lost to follow-up	3

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: From the overall enrolled 319 patients, 56 patients were not randomized and therefore were excluded from the trial. Out of 263 randomized patients, 36 were not exposed to any trial treatment, thus comprising a safety analysis set of 227 patients. 10 patients of the safety set were not eligible and were therefore excluded from the ITT analysis.

Baseline characteristics

Reporting groups

Reporting group title	Low Cell Count (CL1)
Reporting group description: In this arm 0.2 x 10e6 autologous skeletal muscle-derived cells (Low Cell Count) are implanted in female patients with stress urinary incontinence.	
Reporting group title	High cell count (CL2)
Reporting group description: In this arm 10 x 10e6 autologous skeletal muscle-derived cells (Low Cell Count) are implanted in female patients with stress urinary incontinence.	
Reporting group title	Duloxetine-placebo (C1)
Reporting group description: Placebo (for Duloxetine arm)	
Reporting group title	Duloxetine (C2)
Reporting group description: Duloxetine with increasing concentration over the weeks of application was administered in this arm	

Reporting group values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)
Number of subjects	64	56	72
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	54.4 ± 13.1	55.2 ± 11.1	58.1 ± 11.7
Gender categorical Units: Subjects			
Female	64	56	72
Male	0	0	0

Reporting group values	Duloxetine (C2)	Total	
Number of subjects	35	227	
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	61.6 ± 11.8	-	
Gender categorical Units: Subjects			
Female	35	227	
Male	0	0	

End points

End points reporting groups

Reporting group title	Low Cell Count (CL1)
Reporting group description: In this arm 0.2 x 10e6 autologous skeletal muscle-derived cells (Low Cell Count) are implanted in female patients with stress urinary incontinence.	
Reporting group title	High cell count (CL2)
Reporting group description: In this arm 10 x 10e6 autologous skeletal muscle-derived cells (Low Cell Count) are implanted in female patients with stress urinary incontinence.	
Reporting group title	Duloxetine-placebo (C1)
Reporting group description: Placebo (for Duloxetine arm)	
Reporting group title	Duloxetine (C2)
Reporting group description: Duloxetine with increasing concentration over the weeks of application was administered in this arm	

Primary: Change of IEF of Visit 2 from baseline (Visit -5)

End point title	Change of IEF of Visit 2 from baseline (Visit -5)
End point description: The frequency of incontinence episodes were documented by a bowel diary that was completed by the patient. In this study, the frequency of incontinence episodes was calculated as the number of incontinence episodes over 7 days.	
End point type	Primary
End point timeframe: Changes in IEF at Visit 2 (42 days post implantation) compared to baseline Visit -5 (49 days prior implantation) in each treatment group.	

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	56	68	32
Units: IEF change				
arithmetic mean (standard deviation)	-15.5 (± 12)	-15.7 (± 17.5)	-8.6 (± 10.7)	-12.1 (± 12.4)

Statistical analyses

Statistical analysis title	High Cell Count (CL2) vs. Placebo (C1)
Statistical analysis description: The treatment groups were tested by using a two-sided t-test for the hypotheses and two-sided parametric confidence intervals. A sequentially rejective multiple test procedure on a family-wise error rate of $\alpha_{\text{global}} = 0.05$ was used.	
Comparison groups	High cell count (CL2) v Duloxetine-placebo (C1)

Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0097
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Variability estimate	Standard deviation

Statistical analysis title	Low Cell Count (CL1) vs. Placebo (C1)
Comparison groups	Low Cell Count (CL1) v Duloxetine-placebo (C1)
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Variability estimate	Standard deviation

Statistical analysis title	High Cell Count (CL2) vs. Low Cell Count(CL1)
Comparison groups	Low Cell Count (CL1) v High cell count (CL2)
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9282
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Variability estimate	Standard deviation

Statistical analysis title	Copy of High Cell Count (CL2) vs. Placebo (C1)
Statistical analysis description: The treatment groups were tested by using a two-sided t-test for the hypotheses and two-sided parametric confidence intervals. A sequentially rejective multiple test procedure on a family-wise error rate of $\alpha_{\text{global}} = 0.05$ was used.	
Comparison groups	High cell count (CL2) v Duloxetine-placebo (C1)
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0097
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Variability estimate	Standard deviation

Primary: Change of IEF of Visit 3 from baseline (Visit -5)

End point title	Change of IEF of Visit 3 from baseline (Visit -5)
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End point description:

The frequency of incontinence episodes were documented by a bowel diary that was completed by the patient. In this study, the frequency of incontinence episodes was calculated as the number of incontinence episodes over 7 days.

End point type	Primary
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End point timeframe:

Changes in IEF at Visit 3 (84 days post implantation) compared to baseline Visit -5 (49 days prior implantation) in each treatment group.

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: IEF change				
arithmetic mean (standard deviation)	-16.4 (± 13.3)	-18.4 (± 18.6)	-9 (± 13.1)	-13.8 (± 15.9)

Statistical analyses

Statistical analysis title	High Cell Count (CL2) vs. Placebo (C1)
Comparison groups	High cell count (CL2) v Duloxetine-placebo (C1)
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Variability estimate	Standard deviation

Statistical analysis title	Low Cell Count (CL1) vs. Placebo (C1)
Comparison groups	Low Cell Count (CL1) v Duloxetine-placebo (C1)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0019
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Variability estimate	Standard deviation

Statistical analysis title	High Cell Count (CL2) vs. Low Cell Count(CL1)
Comparison groups	High cell count (CL2) v Low Cell Count (CL1)

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5064
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Variability estimate	Standard deviation

Secondary: Change of visual analogue scale (VAS) of Visit 2 from baseline Visit -5

End point title	Change of visual analogue scale (VAS) of Visit 2 from baseline Visit -5
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End point description:

The individual perception of UI complaints will be evaluated by each patient using a standardized VAS. The VAS is an instrument that measures a characteristic or attitude believed to range across a continuum of values and cannot easily be directly measured. It is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patient should mark the VAS with a vertical line representing his or her perception of the individual UI status. In the study, the two endpoints of the VAS are defined as "no complaints at all" (0 cm) and "worst complaints imaginable" (10 cm).

End point type	Secondary
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End point timeframe:

Changes of visual analogue scale (VAS) from Visit 2 (42 days post implantation) compared to baseline Visit -5 (49 day prior implantation) in each treatment group.

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: cm				
arithmetic mean (standard deviation)	-2.0 (± 2)	-1.6 (± 2.2)	-1.0 (± 1.8)	-1.3 (± 1.6)

Statistical analyses

Statistical analysis title	High Cell Count (CL2) vs. Placebo (C1)
Comparison groups	High cell count (CL2) v Duloxetine-placebo (C1)
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.1178
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - ITT/LOCF

Statistical analysis title	Low Cell Count (CL1) vs. Placebo (C1)
Comparison groups	Low Cell Count (CL1) v Duloxetine-placebo (C1)

Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other ^[2]
P-value	= 0.0054
Method	Wilcoxon (Mann-Whitney)

Notes:

[2] - ITT/LOCF

Statistical analysis title	High Cell Count (CL2) vs. Low Cell Count(CL1)
Comparison groups	Low Cell Count (CL1) v High cell count (CL2)
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	= 0.2788
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - ITT/LOCF

Statistical analysis title	High Cell Count (CL2) vs. Duloxetine (C2)
Comparison groups	High cell count (CL2) v Duloxetine (C2)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other ^[4]
P-value	= 0.6519
Method	Wilcoxon (Mann-Whitney)

Notes:

[4] - ITT/LOCF

Statistical analysis title	Low Cell Count (CL1) vs. Duloxetine
Comparison groups	Low Cell Count (CL1) v Duloxetine-placebo (C1)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other ^[5]
P-value	= 0.1346
Method	Wilcoxon (Mann-Whitney)

Notes:

[5] - ITT/LOCF

Statistical analysis title	Placebo (C1) vs. Duloxetine (C2)
Comparison groups	Duloxetine (C2) v Duloxetine-placebo (C1)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other ^[6]
P-value	= 0.3872 ^[7]
Method	Wilcoxon (Mann-Whitney)

Notes:

[6] - ITT/LOCF

[7] - ITT/LOCF

Secondary: Change of visual analogue scale (VAS) of Visit 3 from baseline Visit -5

End point title	Change of visual analogue scale (VAS) of Visit 3 from baseline Visit -5
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End point description:

The individual perception of UI complaints will be evaluated by each patient using a standardized VAS. The VAS is an instrument that measures a characteristic or attitude believed to range across a continuum of values and cannot easily be directly measured. It is usually a horizontal line, 100 mm in length, anchored by word descriptors at each end. The patient should mark the VAS with a vertical line representing his or her perception of the individual UI status. In the study, the two endpoints of the VAS are defined as "no complaints at all" (0 cm) and "worst complaints imaginable" (10 cm).

End point type	Secondary
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End point timeframe:

Changes of visual analogue scale (VAS) from Visit 3 (84 days post implantation) compared to baseline Visit -5 (49 day prior implantation) in each treatment group.

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: cm				
arithmetic mean (standard deviation)	-2.0 (\pm 2.5)	-1.9 (\pm 2.4)	-1.4 (\pm 2.1)	-1.6 (\pm 1.9)

Statistical analyses

Statistical analysis title	High Cell Count (CL2) vs. Placebo (C1)
Comparison groups	Duloxetine-placebo (C1) v High cell count (CL2)
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3961
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Low Cell Count (CL1) vs. Placebo (C1)
Comparison groups	Low Cell Count (CL1) v Duloxetine-placebo (C1)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1388
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	High Cell Count (CL2) vs. Low Cell Count (CL1)
Comparison groups	Low Cell Count (CL1) v High cell count (CL2)

Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.476
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Placebo (C1) vs. Duloxetine (C2)
Comparison groups	Duloxetine-placebo (C1) v Duloxetine (C2)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6736
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	High Cell Count (CL2) vs. Duloxetine (C2)
Comparison groups	High cell count (CL2) v Duloxetine (C2)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.798
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Low Cell Count (CL1) vs. Duloxetine
Comparison groups	Low Cell Count (CL1) v Duloxetine (C2)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4884
Method	Wilcoxon (Mann-Whitney)

Secondary: Incontinence Episode Frequency Reduction $\geq 50\%$ (V2 compared to V-5)

End point title	Incontinence Episode Frequency Reduction $\geq 50\%$ (V2 compared to V-5)
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End point description:

The Incontinence Episodes Frequency (IEF) is calculated as number of incontinence episodes that occurred during 7 days preceding a visit.

End point type	Secondary
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End point timeframe:

Frequency of response measured as a reduction of the frequency of incontinence episodes by more than 50% under treatment from V2 compared to V-5 (baseline).

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	47	42	25	18

Statistical analyses

No statistical analyses for this end point

Secondary: Incontinence Episode Frequency Reduction $\geq 50\%$ (V3 compared to V-5)

End point title	Incontinence Episode Frequency Reduction $\geq 50\%$ (V3 compared to V-5)
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End point description:

The Incontinence Episodes Frequency (IEF) is calculated as number of incontinence episodes that occurred during 7 days preceding a visit.

End point type	Secondary
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End point timeframe:

Frequency of response measured as a reduction of the frequency of incontinence episodes by more than 50% under treatment from V3 compared to V-5 (baseline).

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	46	45	30	17

Statistical analyses

No statistical analyses for this end point

Secondary: Incontinence Episode Frequency Reduction $\geq 75\%$ (V2 compared to V-5)

End point title	Incontinence Episode Frequency Reduction $\geq 75\%$ (V2 compared to V-5)
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End point description:

The Incontinence Episodes Frequency (IEF) is calculated as number of incontinence episodes that occurred during 7 days preceding a visit.

End point type	Secondary
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End point timeframe:

Frequency of response measured as a reduction of the frequency of incontinence episodes by more than 75% under treatment from V2 compared to V-5 (baseline).

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	32	22	14	9

Statistical analyses

No statistical analyses for this end point

Secondary: Incontinence Episode Frequency Reduction $\geq 75\%$ (V3 compared to V-5)

End point title	Incontinence Episode Frequency Reduction $\geq 75\%$ (V3 compared to V-5)
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End point description:

The Incontinence Episodes Frequency (IEF) is calculated as number of incontinence episodes that occurred during 7 days preceding a visit.

End point type	Secondary
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End point timeframe:

Frequency of response measured as a reduction of the frequency of incontinence episodes by more than 75% under treatment from V3 compared to V-5 (baseline).

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	37	28	18	9

Statistical analyses

No statistical analyses for this end point

Secondary: Short-Pad Test Results (V2 compared to Screening)

End point title	Short-Pad Test Results (V2 compared to Screening)
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End point description:

The short-pas test is used to quantify urine leakage in patientes suffering from UI. The change in the pad weight of a patient was calculated by visit based on the weights prior and after the short-pad test.

End point type	Secondary
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End point timeframe:

Difference of pad weight (grams) of V2 compared to screening visit (56 day prior to treatment).

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	56	68	32
Units: gram(s)				
arithmetic mean (standard deviation)	-9.9 (± 8.5)	-9.5 (± 9)	-5.3 (± 7.9)	-7.5 (± 10)

Statistical analyses

No statistical analyses for this end point

Secondary: Short-Pad Test Results (V3 compared to Screening)

End point title	Short-Pad Test Results (V3 compared to Screening)
End point description: The short-pas test is used to quantify urine leakage in patientes suffering from UI. The change in the pad weight of a patient was calculated by visit based on the weights prior and after the short-pad test.	
End point type	Secondary
End point timeframe: Difference of pad weight (grams) of V3 compared to Screening (56 day prior to treatment).	

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	56	68	32
Units: gram(s)				
arithmetic mean (standard deviation)	-10.9 (± 9)	-11.3 (± 8.1)	-6.7 (± 9.4)	-6.8 (± 11.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Incontinence Quality of Life (I-QoL) (V2 compared to V-5)

End point title	Incontinence Quality of Life (I-QoL) (V2 compared to V-5)
End point description: The patients' health-related QoL is assessed using the urinary I-QoL scale with 22-items specific to people with stress and mixed types of UI. It includes general questions on eliciting all areas of concern and specific probes into hypothesized areas of impact: social life, family life, job/work, intimate relationships, activities of daily life, household activities recreation and travel, mental health, physical health, and anxiety/depression.	
End point type	Secondary

End point timeframe:

Change of Patient's assessment based on the Quality of Life questionnaire (QoL) lifestyle score of V2 compared to baseline (V-5) in each treatment group

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: I-QoL total score				
arithmetic mean (standard deviation)	26.5 (\pm 23.4)	28.5 (\pm 20.3)	12.1 (\pm 20.3)	14.2 (\pm 15.5)

Statistical analyses

Statistical analysis title	High Cell Count (CL2) vs. Placebo (C1)
Comparison groups	High cell count (CL2) v Duloxetine-placebo (C1)
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Low Cell Count (CL1) vs. Placebo (C1)
Comparison groups	Low Cell Count (CL1) v Duloxetine-placebo (C1)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0007
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	High Cell Count (CL2) vs. Low Cell Count(CL1)
Comparison groups	High cell count (CL2) v Low Cell Count (CL1)
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5667
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Low Cell Count (CL1) vs. Duloxetine
Comparison groups	Low Cell Count (CL1) v Duloxetine-placebo (C1)

Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0134
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Placebo (C1) vs. Duloxetine (C2)
Comparison groups	Duloxetine-placebo (C1) v Duloxetine (C2)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4836
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	High Cell Count (CL2) vs. Duloxetine (C2)
Comparison groups	High cell count (CL2) v Duloxetine (C2)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0008
Method	Wilcoxon (Mann-Whitney)

Secondary: Incontinence Quality of Life (I-QoL) (V3 compared to V-5)

End point title	Incontinence Quality of Life (I-QoL) (V3 compared to V-5)
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End point description:

The patients' health-related QoL is assessed using the urinary I-QoL scale with 22-items specific to people with stress and mixed types of UI. It includes general questions on eliciting all areas of concern and specific probes into hypothesized areas of impact: social life, family life, job/work, intimate relationships, activities of daily life, household activities recreation and travel, mental health, physical health, and anxiety/depression.

End point type	Secondary
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End point timeframe:

Change of Patient's assessment based on the Quality of Life questionnaire (QoL) lifestyle score of V3 compared to baseline (V-5) in each treatment group.

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: I-QoL total score				
arithmetic mean (standard deviation)	31.3 (± 25.3)	32.3 (± 21.3)	13.8 (± 22.1)	20.2 (± 17.8)

Statistical analyses

Statistical analysis title	High Cell Count (CL2) vs. Placebo (C1)
Comparison groups	High cell count (CL2) v Duloxetine-placebo (C1)
Number of subjects included in analysis	124
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Low Cell Count (CL1) vs. Placebo (C1)
Comparison groups	Low Cell Count (CL1) v Duloxetine-placebo (C1)
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0002
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	High Cell Count (CL2) vs. Low Cell Count (CL1)
Comparison groups	Low Cell Count (CL1) v High cell count (CL2)
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6985
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Placebo (C1) vs. Duloxetine (C2)
Comparison groups	Duloxetine-placebo (C1) v Duloxetine (C2)
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1284
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	High Cell Count (CL2) vs. Duloxetine (C2)
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Comparison groups	High cell count (CL2) v Duloxetine (C2)
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0094
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Low Cell Count (CL1) vs. Duloxetine
Comparison groups	Low Cell Count (CL1) v Duloxetine (C2)
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0438
Method	Wilcoxon (Mann-Whitney)

Secondary: Clinical Global Impression (CGI) improvement: very much improved

End point title	Clinical Global Impression (CGI) improvement: very much improved
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.

End point type	Secondary
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End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V3.

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	56	68	32
Units: Number of Patients	29	21	8	5

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: much improved

End point title	Clinical Global Impression (CGI) improvement: much improved
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End point description:

Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side

effects. The CGI scale is widely used in clinical studies as an outcome measure.

End point type	Secondary
End point timeframe:	
Investigator's assessment by the Clinical Global Impression (CGI-I) score at V3.	

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	14	22	12	7

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: minimally improved

End point title	Clinical Global Impression (CGI) improvement: minimally improved
End point description:	
Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.	
End point type	Secondary
End point timeframe:	
Investigator's assessment by the Clinical Global Impression (CGI-I) score at V3.	

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	8	8	13	7

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: no change

End point title	Clinical Global Impression (CGI) improvement: no change
End point description:	
Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.	

End point type	Secondary
End point timeframe:	
Investigator's assessment by the Clinical Global Impression (CGI-I) score at V	

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	8	2	19	5

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: minimally worse

End point title	Clinical Global Impression (CGI) improvement: minimally worse
End point description:	
Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.	
End point type	Secondary
End point timeframe:	
Investigator's assessment by the Clinical Global Impression (CGI-I) score at V3.	

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	1	1	3	1

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) improvement: much worse

End point title	Clinical Global Impression (CGI) improvement: much worse
End point description:	
Improvement of urinary incontinence was assessed using the Clinical Global Impression Scale, which is a standardized assessment tool that allows the physician to rate the severity of illness, change over time, and efficiency of treatment, taking into account the patient's clinical condition and the severity of side effects. The CGI scale is widely used in clinical studies as an outcome measure.	
End point type	Secondary

End point timeframe:

Investigator's assessment by the Clinical Global Impression (CGI-I) score at V3.

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	56	68	32
Units: Number of Patients	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Urinary volume lost during incontinence episodes (V3 compared to V-5)

End point title	Urinary volume lost during incontinence episodes (V3 compared to V-5)
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End point description:

The volume of micturition episodes of a patient was determined using diary entries for the last three days prior to a visit.

End point type	Secondary
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End point timeframe:

Difference of voiding volume during incontinence episodes of V3 compared to baseline (V-5).

End point values	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)	Duloxetine (C2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	56	68	32
Units: mL				
arithmetic mean (standard deviation)	-13.1 (± 75.08)	-5.9 (± 55.66)	1 (± 51.22)	4.5 (± 59.26)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

June 2010 - June 2011

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.1
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Reporting groups

Reporting group title	Low Cell Count (CL1)
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Reporting group description:

227 patients compsoe the safety set. 133 patients of the safety set underwent biopsy and cell implatation. 72 patients received no treatment.

Reporting group title	High cell count (CL2)
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Reporting group description:

227 patients compsoe the safety set. 133 patients of the safety set underwent biopsy and cell implatation. 72 patients received no treatment.

Reporting group title	Duloxetine-placebo (C1)
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Reporting group description:

227 patients compsoe the safety set. 133 patients of the safety set underwent biopsy and cell implatation. 72 patients received no treatment.

Reporting group title	Duloxetine (C2)
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Reporting group description:

227 patients compsoe the safety set. 133 patients of the safety set underwent biopsy and cell implatation. 72 patients received no treatment.

Serious adverse events	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 64 (7.81%)	3 / 56 (5.36%)	4 / 72 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	1 / 64 (1.56%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Tachyarrhythmia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	1 / 64 (1.56%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 64 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial insufficiency			
subjects affected / exposed	0 / 64 (0.00%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Post procedural haemorrhage			
subjects affected / exposed	1 / 64 (1.56%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Post-traumatic headache			
subjects affected / exposed	1 / 64 (1.56%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 64 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular disorder			

subjects affected / exposed	1 / 64 (1.56%)	0 / 56 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 64 (0.00%)	0 / 56 (0.00%)	1 / 72 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 56 (1.79%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Hepatitis B			
subjects affected / exposed	0 / 64 (0.00%)	1 / 56 (1.79%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Duloxetine (C2)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 35 (2.86%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Tachyarrhythmia			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest discomfort			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arterial insufficiency			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Post procedural haemorrhage			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Post-traumatic headache			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vestibular disorder			
subjects affected / exposed	0 / 35 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Immune system disorders Allergy to arthropod bite subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 35 (0.00%) 0 / 0 0 / 0		
Respiratory, thoracic and mediastinal disorders Pneumonitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 35 (0.00%) 0 / 0 0 / 0		
Infections and infestations Hepatitis B subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 35 (0.00%) 0 / 0 0 / 0		

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

Non-serious adverse events	Low Cell Count (CL1)	High cell count (CL2)	Duloxetine-placebo (C1)
Total subjects affected by non-serious adverse events subjects affected / exposed	17 / 64 (26.56%)	20 / 56 (35.71%)	33 / 72 (45.83%)
Vascular disorders All PT's in this SOC subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1	1 / 56 (1.79%) 1	10 / 72 (13.89%) 11
Surgical and medical procedures All PT's in this SOC subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1	0 / 56 (0.00%) 0	0 / 72 (0.00%) 0
General disorders and administration site conditions All PT's in this SOC subjects affected / exposed occurrences (all)	2 / 64 (3.13%) 4	0 / 56 (0.00%) 0	3 / 72 (4.17%) 4
Reproductive system and breast disorders			

All PT's in this SOC subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1	3 / 56 (5.36%) 3	1 / 72 (1.39%) 1
Respiratory, thoracic and mediastinal disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	3 / 56 (5.36%) 3	3 / 72 (4.17%) 4
Psychiatric disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	0 / 56 (0.00%) 0	3 / 72 (4.17%) 3
Investigations All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	1 / 56 (1.79%) 1	5 / 72 (6.94%) 5
Injury, poisoning and procedural complications All PT's in this SOC subjects affected / exposed occurrences (all)	3 / 64 (4.69%) 3	1 / 56 (1.79%) 1	2 / 72 (2.78%) 3
Cardiac disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	1 / 56 (1.79%) 1	4 / 72 (5.56%) 5
Nervous system disorders All PT's in this SOC subjects affected / exposed occurrences (all)	2 / 64 (3.13%) 2	1 / 56 (1.79%) 2	9 / 72 (12.50%) 13
Eye disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	0 / 56 (0.00%) 0	1 / 72 (1.39%) 1
Gastrointestinal disorders All PT's in this SOC subjects affected / exposed occurrences (all)	3 / 64 (4.69%) 4	2 / 56 (3.57%) 2	14 / 72 (19.44%) 21
Hepatobiliary disorders			

All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	0 / 56 (0.00%) 0	2 / 72 (2.78%) 2
Skin and subcutaneous tissue disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	0 / 56 (0.00%) 0	2 / 72 (2.78%) 2
Renal and urinary disorders All PT's in this SOC subjects affected / exposed occurrences (all)	7 / 64 (10.94%) 8	5 / 56 (8.93%) 6	0 / 72 (0.00%) 0
Musculoskeletal and connective tissue disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	1 / 56 (1.79%) 1	2 / 72 (2.78%) 2
Infections and infestations All PT's in this SOC subjects affected / exposed occurrences (all)	4 / 64 (6.25%) 6	7 / 56 (12.50%) 7	5 / 72 (6.94%) 8
Metabolism and nutrition disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 64 (0.00%) 0	0 / 56 (0.00%) 0	1 / 72 (1.39%) 2

Non-serious adverse events	Duloxetine (C2)		
Total subjects affected by non-serious adverse events subjects affected / exposed	15 / 35 (42.86%)		
Vascular disorders All PT's in this SOC subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 2		
Surgical and medical procedures All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
General disorders and administration site conditions All PT's in this SOC			

subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Reproductive system and breast disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Psychiatric disorders All PT's in this SOC subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Investigations All PT's in this SOC subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Injury, poisoning and procedural complications All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Cardiac disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Nervous system disorders All PT's in this SOC subjects affected / exposed occurrences (all)	6 / 35 (17.14%) 6		
Eye disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Gastrointestinal disorders			

All PT's in this SOC subjects affected / exposed occurrences (all)	11 / 35 (31.43%) 16		
Hepatobiliary disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Skin and subcutaneous tissue disorders All PT's in this SOC subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 2		
Renal and urinary disorders All PT's in this SOC subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1		
Musculoskeletal and connective tissue disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		
Infections and infestations All PT's in this SOC subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2		
Metabolism and nutrition disorders All PT's in this SOC subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 January 2010	<ul style="list-style-type: none">- Change of Study duration in total and per patient, prolongation of screening period and cell preparation- Change of patients planned for a 9 month follow up study (only patients with a decrease of at least 25% in the IEF score)- Addition of age limits for Germany and CZ- Addition of Inclusion Criterion (female patients willing to use acceptable methods of contraception)- Addition of Interim Inclusion Criterion (patients with an IEF of at least 12 within the last 7 days prior baseline)- Addition of Exclusion Criterion 23, 24, 25 (patients with malignant disease, with chronic bacterial infections, or with hypersensitivity to any component of the product)- Introduction of a randomization list and addition of detailed description of the randomization process and unblinding
27 January 2010	Addition of Exclusion Criterion No. 24
10 June 2010	Changes based on a new IMPD
08 July 2010	Follow up will be extended to all patients
13 August 2010	Interim Analysis is introduced.
27 September 2010	Overall study duration is introduced due to prolonged patient recruitment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported