Clinical trial results:
Combined Randomized, Double-Blind, Dose-Confirming Phase 3a Study in Parallel Design to Assess the Efficacy and Safety of Topical 4-Week Treatment With 1% GPB Cream vs Placebo and Open-Label Phase 3b Study to Assess Long-Term Efficacy and Safety in Patients With Primary Axillary Hyperhidrosis Treated With 1% GPB Cream

Summary

EudraCT number	2017-004534-28
Trial protocol	DE SE GB AT HU DK PL
Global end of trial date	02 February 2022

Results information

Result version number	v2 (current)
This version publication date	15 April 2023
First version publication date	25 December 2022
Version creation reason	• Correction of full data set Correction of Global end of trial date

Trial information

Trial identification

Sponsor protocol code	Hyp1-18/2016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03658616
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dr. August Wolff GmbH & Co. KG Arzneimittel
Sponsor organisation address	Sudbrackstr. 56, Bielefeld, Germany, 33611
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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	17 February 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2021
Global end of trial reached?	Yes
Global end of trial date	02 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The assessment of efficacy and safety of topical administration of 1% GPB or placebo cream in patients with primary axillary hyperhidrosis, and the assessment of long-term efficacy and safety of topical administration of 1% GPB cream in patients with primary axillary hyperhidrosis.

Protection of trial subjects:

This study was in compliance with the ethical principles of current applicable regulations, International Council for Harmonisation (ICH) of Good Clinical Practice, the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements. All regulatory requirements relevant to the safety of the study participants were followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	17 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 72
Country: Number of subjects enrolled	Sweden: 116
Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	Germany: 273
Country: Number of subjects enrolled	Hungary: 35
Worldwide total number of subjects	528
EEA total number of subjects	511

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)	526
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Men and woman between 18 to 65 years with a body mass index of 18-32 kg/m2 that were diagnosed with severe primary axillary hyperhidrosis scoring a 3 or 4 in hyperhidrosis disease severity were recruited for the study. Recruitment took place for the dose-confirming part (3a) and subsequently for the long-term part (3b).

Pre-assignment

Screening details:

For part 3a, 171 out of 272 screened patients fulfilled the criteria of at least 50 mg sweat production in each axilla after a 14-day washout phase of previously used antiperspirants. For part 3b, 161 patients rolled over from part 3a and 357 out of 566 newly screened patients were also recruited fulfilling the selection critera.

Period 1

Period 1 title	Dose-confirming part (Phase 3a)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Assessor, Subject

Blinding implementation details:

To maintain the blind, GPB and placebo cream had identical appearance, texture, smell, as well as identical labeling and packaging. To minimize the potential for bias, treatment randomization information was kept confidential by the responsible sponsor personnel and was disclosed to the investigator, other study center personnel, the sponsor or its designee, and clinical research associate until after database lock.

Arms

Are arms mutually exclusive?	Yes
Arm title	1% glycopyrronium bromide (GPB) cream

Arm description:

In the dose-confirming Phase 3a part, 171 patients were randomized in a 1:1 ratio to once-daily treatment with 1% GPB cream (87 patients) or placebo cream (84 patients) for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	1% GPB cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Topical administration to both axillae, once daily for 4 weeks starting on Day 1a. After Week 4 topical administration as needed (at least twice per week and at most once daily).

Arm title	Placebo cream

Arm description:

The placebo cream was used in the Phase 3a part only and was identical to the GPB cream in terms of appearance, constitution of excipients, and packaging but was lacking active substance.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Topical administration to both axillae, once daily for 4 weeks starting on Day 1a.

Number of subjects in period 1[1]	1% glycopyrronium bromide (GPB) cream	Placebo cream
Started	87	84
Completed	84	82
Not completed	3	2
Consent withdrawn by subject	1	-
Lost to follow-up	1	1
Lack of efficacy	1	1

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: The study consists of part 3a and 3b. Part 3a includes 171 patients and part 3b includes 357 newly recruited patients, for a total of 528 patients. Part 3a and 3b each has a baseline (Day 1a and Day 1b). For technical reasons, we only can report one baseline period.

Period 2

Period 2 title	Long-term part (Phase 3b)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

The long-term part of the study was open-label; thus, no randomization or blinding was done.

Arms

Arm title	1% glycopyrronium bromide (GPB) cream

Arm description:

During the Phase 3b part, patients were treated with 1% GPB cream for up to 72 weeks. Newly recruited patients applied 1% GPB cream once daily for the first 4 weeks (analogous to the treatment applied during Phase 3a). After the first 4 weeks of treatment (ie, after completion of Week 4), all patients (including those who rolled-over from the Phase 3a part) applied 1% GPB cream as needed (at least twice per week but at most once daily) up to Week 72/EOTb, followed by a 4-week safety follow-up.

Arm type	Experimental
Investigational medicinal product name	1% glycopyrronium bromide
Investigational medicinal product code	1% GPB cream
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Topical administration to both axillae. Newly recruited patients applied 1% GPB cream once daily for the first 4 weeks (analogous to the treatment applied during Phase 3a). After the first 4 weeks of treatment (ie, after completion of Week 4), all patients (including those who rolled-over from the Phase 3a part) applied 1% GPB cream as needed (at least twice a week, but at most once daily) up to Week 72.

Number of subjects in period 2[2]	1% glycopyrronium bromide (GPB) cream
Started	161
Completed	368
Not completed	150
Adverse event, non-fatal	15
Death	1
Other reasons	36
Lost to follow-up	43
Consent withdrawn by subject	55
Joined	357
Late recruitment	357
Late recruitment reason	To achieve the planned total of 500 patients for the long-term 3b part of the study (including roll-over patients from Phase 3a), 357 additional patients were enrolled at Visit 3b (Baseline of long-term part).

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The study consists of part 3a and 3b. Part 3a includes 171 patients and part 3b includes 357 newly recruited patients, for a total of 528 patients. Part 3a and 3b each has a baseline (Day 1a and Day 1b). For technical reasons, we only can report one baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	1% glycopyrronium bromide (GPB) cream
Reporting group description:	
In the dose-confirming Phase 3a part, 171 patients were randomized in a 1:1 ratio to once-daily treatment with 1% GPB cream (87 patients) or placebo cream (84 patients) for 4 weeks.	
Reporting group title	Placebo cream
Reporting group description:	
The placebo cream was used in the Phase 3a part only and was identical to the GPB cream in terms of appearance, constitution of excipients, and packaging but was lacking active substance.	

Reporting group values	1% glycopyrronium bromide (GPB) cream	Placebo cream	Total
Number of subjects	87	84	171
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults (18-65 years)	87	84	171
Age continuous Units: years			
arithmetic mean	37.4	37.8	
standard deviation	± 11.9	± 12.3	-
Gender categorical Units: Subjects			
Female	43	41	84
Male	44	43	87

Subject analysis sets	
Subject analysis set title	1% GPB (SAFa)
Subject analysis set type	Safety analysis
Subject analysis set description:	
The SAFa includes all patients who received at least 1 dose of IMP in Phase 3a. The assignment of patients to the treatment groups was as actually treated. The SAFa was used for all safety analyses of Phase 3a.	
Subject analysis set title	1% GPB (FASa)
Subject analysis set type	Full analysis
Subject analysis set description:	
The FASa includes all patients randomized and treated at least once with IMP in Phase 3a. As per the intention-to-treat principle, the assignment of patients to the treatment groups was as randomized. The	

FASa was used for the evaluation of all efficacy endpoints of Phase 3a.

Subject analysis set title	1% GPB (PPSa)
Subject analysis set type	Per protocol

Subject analysis set description:

The PPSa includes all patients of the FASa without any major protocol deviations in Phase 3a. The assignment of patients to the treatment groups was as actually treated. Protocol deviations were reviewed during a blind data review meeting (BDRM) held before the data base lock and unblinding of the Phase 3a part data to identify major deviations leading to the exclusion of patients from the PPSa.

Subject analysis set title	Placebo (SAFa)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAFa includes all patients who received at least 1 dose of IMP in Phase 3a. The assignment of patients to the treatment groups was as actually treated. The SAFa was used for all safety analyses of Phase 3a.

Subject analysis set title	Placebo (FASa)
Subject analysis set type	Full analysis

Subject analysis set description:

The FASa includes all patients randomized and treated at least once with IMP in Phase 3a. As per the intention-to-treat principle, the assignment of patients to the treatment groups was as randomized. The FASa was used for the evaluation of all efficacy endpoints of Phase 3a.

Subject analysis set title	Placebo (PPSa)
Subject analysis set type	Per protocol

Subject analysis set description:

The PPSa includes all patients of the FASa without any major protocol deviations in Phase 3a. The assignment of patients to the treatment groups was as actually treated. Protocol deviations were reviewed during a blind data review meeting (BDRM) held before the data base lock and unblinding of the Phase 3a part data to identify major deviations leading to the exclusion of patients from the PPSa.

Subject analysis set title	1% GPB (SAFb)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAFb includes all patients treated at least once with IMP in the Phase 3b part of the study (ie, roll-over patients from the Phase 3a and patients newly recruited to the Phase 3b part) and was used for all safety analyses of Phase 3b.

Subject analysis set title	1% GPB (FASb)
Subject analysis set type	Full analysis

Subject analysis set description:

The FASb includes all patients of the SAFb

Subject analysis set title	1% GPB (FASnewb)
Subject analysis set type	Full analysis

Subject analysis set description:

The FASnewb includes all patients newly recruited to the Phase 3b part who were treated at least once with IMP. This set is a subset of the FASb and was used for the evaluation of the primary and all secondary endpoints regarding only newly recruited patients. The FASb was used for all other secondary endpoint analyses.

Subject analysis set title	1% GPB (PPSb)
Subject analysis set type	Per protocol

Subject analysis set description:

The PPSb or PPSnewb includes all patients of the FASb or FASnewb who had no major protocol deviations until Week 28. No analyses using the PPSb or PPSnewb were planned after Week 28. Protocol deviations were reviewed during a DRM held before the final data base lock to identify major deviations leading to the exclusion of patients from the PPSb or PPSnewb.

Subject analysis set title	1% GPB (PPSnewb)
Subject analysis set type	Per protocol

Subject analysis set description:

1% GPB PPSnewb includes all patients of the FASb or FASnewb who had no major protocol deviations until Week 28

Reporting group values	1% GPB (SAFa)	1% GPB (FASa)	1% GPB (PPSa)
Number of subjects	87	87	69
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults (18-65 years)	87	87	69
Age continuous Units: years			
arithmetic mean		37.4	
standard deviation	±	± 11.9	±
Gender categorical Units: Subjects			
Female		43	
Male		44	

Reporting group values	Placebo (SAFa)	Placebo (FASa)	Placebo (PPSa)
Number of subjects	84	84	58
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults (18-65 years)	84	84	58
Age continuous Units: years			
arithmetic mean		37.8	
standard deviation	±	± 12.3	±
Gender categorical Units: Subjects			
Female		41	
Male		43	

Reporting group values	1% GPB (SAFb)	1% GPB (FASb)	1% GPB (FASnewb)
Number of subjects	518	518	357

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over Adults (18-65 years)			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female Male			

Reporting group values	1% GPB (PPSb)	1% GPB (PPSnewb)	
Number of subjects	326	205	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over Adults (18-65 years)			
Age continuous Units: years arithmetic mean standard deviation	±	±	
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	1% glycopyrronium bromide (GPB) cream

Reporting group description:

In the dose-confirming Phase 3a part, 171 patients were randomized in a 1:1 ratio to once-daily treatment with 1% GPB cream (87 patients) or placebo cream (84 patients) for 4 weeks.

Reporting group title	Placebo cream

Reporting group description:

The placebo cream was used in the Phase 3a part only and was identical to the GPB cream in terms of appearance, constitution of excipients, and packaging but was lacking active substance.

Reporting group title	1% glycopyrronium bromide (GPB) cream

Reporting group description:

During the Phase 3b part, patients were treated with 1% GPB cream for up to 72 weeks. Newly recruited patients applied 1% GPB cream once daily for the first 4 weeks (analogous to the treatment applied during Phase 3a). After the first 4 weeks of treatment (ie, after completion of Week 4), all patients (including those who rolled-over from the Phase 3a part) applied 1% GPB cream as needed (at least twice per week but at most once daily) up to Week 72/EOTb, followed by a 4-week safety follow-up.

Subject analysis set title	1% GPB (SAFa)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAFa includes all patients who received at least 1 dose of IMP in Phase 3a. The assignment of patients to the treatment groups was as actually treated. The SAFa was used for all safety analyses of Phase 3a.

Subject analysis set title	1% GPB (FASa)
Subject analysis set type	Full analysis

Subject analysis set description:

The FASa includes all patients randomized and treated at least once with IMP in Phase 3a. As per the intention-to-treat principle, the assignment of patients to the treatment groups was as randomized. The FASa was used for the evaluation of all efficacy endpoints of Phase 3a.

Subject analysis set title	1% GPB (PPSa)
Subject analysis set type	Per protocol

Subject analysis set description:

The PPSa includes all patients of the FASa without any major protocol deviations in Phase 3a. The assignment of patients to the treatment groups was as actually treated. Protocol deviations were reviewed during a blind data review meeting (BDRM) held before the data base lock and unblinding of the Phase 3a part data to identify major deviations leading to the exclusion of patients from the PPSa.

Subject analysis set title	Placebo (SAFa)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAFa includes all patients who received at least 1 dose of IMP in Phase 3a. The assignment of patients to the treatment groups was as actually treated. The SAFa was used for all safety analyses of Phase 3a.

Subject analysis set title	Placebo (FASa)
Subject analysis set type	Full analysis

Subject analysis set description:

The FASa includes all patients randomized and treated at least once with IMP in Phase 3a. As per the intention-to-treat principle, the assignment of patients to the treatment groups was as randomized. The FASa was used for the evaluation of all efficacy endpoints of Phase 3a.

Subject analysis set title	Placebo (PPSa)
Subject analysis set type	Per protocol

Subject analysis set description:

The PPSa includes all patients of the FASa without any major protocol deviations in Phase 3a. The assignment of patients to the treatment groups was as actually treated. Protocol deviations were reviewed during a blind data review meeting (BDRM) held before the data base lock and unblinding of the Phase 3a part data to identify major deviations leading to the exclusion of patients from the PPSa.

Subject analysis set title	1% GPB (SAFb)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAFb includes all patients treated at least once with IMP in the Phase 3b part of the study (ie, roll-over patients from the Phase 3a and patients newly recruited to the Phase 3b part) and was used for all safety analyses of Phase 3b.

Subject analysis set title	1% GPB (FASb)
Subject analysis set type	Full analysis

Subject analysis set description:

The FASb includes all patients of the SAFb

Subject analysis set title	1% GPB (FASnewb)
Subject analysis set type	Full analysis

Subject analysis set description:

The FASnewb includes all patients newly recruited to the Phase 3b part who were treated at least once with IMP. This set is a subset of the FASb and was used for the evaluation of the primary and all secondary endpoints regarding only newly recruited patients. The FASb was used for all other secondary endpoint analyses.

Subject analysis set title	1% GPB (PPSb)
Subject analysis set type	Per protocol

Subject analysis set description:

The PPSb or PPSnewb includes all patients of the FASb or FASnewb who had no major protocol deviations until Week 28. No analyses using the PPSb or PPSnewb were planned after Week 28. Protocol deviations were reviewed during a DRM held before the final data base lock to identify major deviations leading to the exclusion of patients from the PPSb or PPSnewb.

Subject analysis set title	1% GPB (PPSnewb)
Subject analysis set type	Per protocol

Subject analysis set description:

1% GPB PPSnewb includes all patients of the FASb or FASnewb who had no major protocol deviations until Week 28

Primary: 3a: Primary efficacy endpoint: Absolute change in total sweat production from Baseline (Day 1a) to Day 29

End point title	3a: Primary efficacy endpoint: Absolute change in total sweat production from Baseline (Day 1a) to Day 29

End point description:

Absolute change in logarithmic values of total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1a) to Day 29 in the 1% GPB group compared to the placebo group. For the dose-confirming part (Phase 3a), the GM of sweat production was performed at the Screening Visit 2a, on Day 1a, and on Day 29/EOTa (Visit 5a).

End point type	Primary

End point timeframe:

Baseline (Day 1a) to Day 29

End point values	1% GPB (FASa)	1% GPB (PPSa)	Placebo (FASa)	Placebo (PPSa)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	77	65	78	55
Units: mg/ 5 min				
log mean (standard deviation)	-1.58 (± 1.87)	-1.40 (± 1.57)	-0.72 (± 1.55)	-0.53 (± 1.21)

Statistical analyses

Statistical analysis title	Absolute change in total sweat production from Bas

Statistical analysis description:

A mixed effects model was used with treatment and logarithmic baseline values as fixed effects and center as random effect to test the primary hypothesis on a significance level of 5% (α=0.05; 2-sided).

Comparison groups	Placebo (FASa) v 1% GPB (FASa)
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Primary: 3b: Primary efficacy endpoint: Absolute change in total sweat production from Baseline (Day 1b) to Week 12

End point title	3b: Primary efficacy endpoint: Absolute change in total sweat production from Baseline (Day 1b) to Week 12

End point description:

Absolute change in logarithmic values of total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1b) to Day 29 in the 1% GPB group compared to the placebo group. For the long-term part of the study (Phase 3b), the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

End point type	Primary

End point timeframe:

Baseline (Day 1b) to Week 12

End point values	1% GPB (FASnewb)	1% GPB (PPSnewb)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	316	198		
Units: mg/ 5 min				
log mean (standard deviation)	-1.529 (± 2.107)	-1.579 (± 2.112)		

Statistical analyses

Statistical analysis title	Titel Endpunkt

Statistical analysis description:

A mixed effects model will be used with mean centered logarithmic baseline values as fixed effects and center as random effect to test the primary hypothesis on a significance level of 2.94% (α=0.0294; 2-sided).

Comparison groups	1% GPB (FASnewb) v 1% GPB (PPSnewb)

Number of subjects included in analysis	514
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.0294
Method	Mixed models analysis

Notes:

[1] - Absolute change from Baseline was analysed

Secondary: 3a: First key secondary endpoint: Percentage of HDSS responders at Day 29

End point title	3a: First key secondary endpoint: Percentage of HDSS responders at Day 29

End point description:

Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

End point type	Secondary

End point timeframe:

Day 29

End point values	1% GPB (FASa)	1% GPB (PPSa)	Placebo (FASa)	Placebo (PPSa)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	87	69	84	58
Units: percentage of patients				
number (not applicable)	23.0	27.5	11.9	12.1

Statistical analyses

No statistical analyses for this end point

Secondary: 3a: Second key secondary endpoint: Absolute change in the HidroQoL from Baseline (Day 1a) to Day 29

End point title	3a: Second key secondary endpoint: Absolute change in the HidroQoL from Baseline (Day 1a) to Day 29

End point description:

The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated.

End point type	Secondary

End point timeframe:

Baseline (Day 1a) to Day 29

End point values	1% GPB (FASa)	1% GPB (PPSa)	Placebo (FASa)	Placebo (PPSa)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	84	69	79	56
Units: Total score				
median (full range (min-max))				
Total score	-6 (-36 to 6)	-6 (-36 to 6)	-1 (-35 to 4)	-1 (-35 to 4)

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: First key secondary endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Week 12 (>25%)

End point title	3b: First key secondary endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Week 12 (>25%)

End point description:

Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

End point type	Secondary

End point timeframe:

Week 12

End point values	1% GPB (FASb)	1% GPB (PPSb)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	518	326		
Units: percentage of patients				
number (not applicable)	28.0	31.6		

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Second key secondary endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Week 28 (>25%)

End point title	3b: Second key secondary endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Week 28 (>25%)

End point description:

Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

End point type	Secondary

End point timeframe:

Week 28

End point values	1% GPB (FASb)	1% GPB (PPSb)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	518	326		
Units: percentage of patients				
number (not applicable)	29.3	35.6		

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Third key secondary endpoint: Absolute change in the HidroQoL from Baseline (Day 1b) to Week 12

End point title	3b: Third key secondary endpoint: Absolute change in the HidroQoL from Baseline (Day 1b) to Week 12

End point description:

The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated.

End point type	Secondary

End point timeframe:

Baseline (Day 1b) to Week 12

End point values	1% GPB (FASb)	1% GPB (PPSb)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	468	321		
Units: Total score				
median (confidence interval 95%)				
Total score	-11 (-13 to -10)	-12 (-13 to -10)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3a: Secondary efficacy endpoint: Absolute change in sweat production assessed by GM from Baseline (Day 1a) to Day 29

End point title	3a: Secondary efficacy endpoint: Absolute change in sweat production assessed by GM from Baseline (Day 1a) to Day 29

End point description:

Absolute change in logarithmic values of total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1a) to Day 29 by treatment group. For the dose-confirming part (Phase 3a), the GM of sweat production was performed at the Screening Visit 2a, on Day 1a, and on Day 29/EOTa (Visit 5a).

End point type	Secondary

End point timeframe:

Baseline (Day 1a) to Day 29

End point values	1% GPB (FASa)	Placebo (FASa)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	78		
Units: mg				
log mean (confidence interval 95%)	-1.58 (-2.01 to -1.16)	-0.72 (-1.07 to -0.37)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3a: Secondary efficacy endpoint: Percentage change in sweat production assessed by GM from Baseline (Day 1a) to Day 29

End point title	3a: Secondary efficacy endpoint: Percentage change in sweat production assessed by GM from Baseline (Day 1a) to Day 29

End point description:

Percentage change of total sweat production from Baseline (Day 1a) to Day 29 by treatment group and in the 1% GPB group compared with the placebo group.

End point type	Secondary

End point timeframe:

Baseline (Day 1a) to Day 29

End point values	1% GPB (FASa)	1% GPB (FASb)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	78		
Units: percent				
median (confidence interval 95%)	-64.63 (-73.13 to -51.75)	-34.32 (-49.71 to -2.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3a: Secondary efficacy endpoint: Percentage of responders assessed by GM on Day 29

End point title	3a: Secondary efficacy endpoint: Percentage of responders assessed by GM on Day 29

End point description:

Responders are defined as patients with at least 50%, 75%, and 90% sweat reduction assessd by gravimetric measurement (GM) compared to Baseline. For this dose-confirming part, the GM of sweat production was performed at the Screening Visit 2a, on Day 1a, and on Day 29/EOTa (Visit 5a).

End point type	Secondary

End point timeframe:

Day 29

End point values	1% GPB (FASa)	Placebo (FASa)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87	84		
Units: percentage of patients				
number (not applicable)				
1. sweat reduction of ≥50%	57.5	34.5		
2. sweat reduction of ≥75%	32.2	16.7		
3. sweat reduction of ≥90%	23.0	9.5		

Statistical analyses

No statistical analyses for this end point

Secondary: 3a: Secondary efficacy endpoint: Absolute change in the HDSS from Baseline (Day 1a) to Day 15 and Day 29

End point title	3a: Secondary efficacy endpoint: Absolute change in the HDSS from Baseline (Day 1a) to Day 15 and Day 29

End point description:

Change of the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

End point type	Secondary

End point timeframe:

Baseline (Day 1a) to Day 15 and to Day 29

End point values	1% GPB (FASa)	Placebo (FASa)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87[2]	84[3]		
Units: score				
median (confidence interval 95%)				
Day 15	-1 (-1 to 0)	0 (0 to 0)		
Day 29	0 (-1 to 0)	0 (0 to 0)		

Notes:

[2] - Day 15: N=84
Day 29: N=83
[3] - Day 15: N=79
Day 29: N=80

Statistical analyses

No statistical analyses for this end point

Secondary: 3a: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS on Day 15

End point title	3a: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS on Day 15

End point description:

Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

End point type	Secondary

End point timeframe:

Day 15

End point values	1% GPB (FASa)	Placebo (FASa)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87	84		
Units: percentage of patients				
number (not applicable)	25.3	9.5		

Statistical analyses

No statistical analyses for this end point

Secondary: 3a: Secondary efficacy endpoint: Absolute change in the HidroQoL from Baseline (Day 1a) to Day 15 and Day 29

End point title	3a: Secondary efficacy endpoint: Absolute change in the HidroQoL from Baseline (Day 1a) to Day 15 and Day 29

End point description:

The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: ‘no, not at all’ = 0, ‘a little’ = 1, and ‘very much’ = 2. A total score was calculated.

End point type	Secondary

End point timeframe:

Baseline (Day 1a) to Day 15 and Day 29

End point values	1% GPB (FASa)	Placebo (FASa)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87[4]	79		
Units: Total score				
median (confidence interval 95%)				
Day 15	-5 (-8 to -2)	-1 (-2 to -1)		
Day 29	-6 (-9 to -4)	-1 (-2 to -1)		

Notes:

[4] - Day 15: N=85
Day 29: N=84

Statistical analyses

No statistical analyses for this end point

Secondary: 3a: Secondary efficacy endpoint: Absolute change in the DLQI from Baseline (Day 1a) to Day 15 and Day 29

End point title	3a: Secondary efficacy endpoint: Absolute change in the DLQI from Baseline (Day 1a) to Day 15 and Day 29

End point description:

The Dermatology Life Quality Index [DLQI] is scored on a 4-point scale: 'very much' = 3, 'a lot' = 2, 'a little' = 1, 'not at all' or 'question not relevant' = 0. It is calculated as sum score of all questions resulting in a total score between 0 and 30. The higher the score, the more the quality of life is impaired.

End point type	Secondary

End point timeframe:

Baseline (Day 1a) to Day 15 and Day 29

End point values	1% GPB (FASa)	Placebo (FASa)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87[5]	79		
Units: score				
median (confidence interval 95%)				
Day 15	-5 (-7 to -2)	-2 (-3 to -1)		
Day 29	-5 (-8 to -4)	-3 (-4 to -1)		

Notes:

[5] - Day 15: N=85
Day 29: N=84

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Percentage change in total sweat production assessed by GM from Baseline (Day 1b) to Week 4 and Week 12

End point title	3b: Secondary efficacy endpoint: Percentage change in total sweat production assessed by GM from Baseline (Day 1b) to Week 4 and Week 12

End point description:

Percentage change in total sweat production assessed by gravimetric measuremt (GM) from Baseline (Day 1b) to Week 4 and Week 12 in the 1% GPB group. For the long-term part of the study (Phase 3b),

the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

End point type	Secondary

End point timeframe:

Baseline (Day 1b) to Week 4 and Week 12

End point values	1% GPB (FASnewb)			
Subject group type	Subject analysis set			
Number of subjects analysed	357[6]			
Units: percent				
median (full range (min-max))				
Week 4	-68.270 (-99.97 to 2100)			
Week 12	-65.630 (-99.97 to 17050)			

Notes:

[6] - Week 4: N=313
Week 12: N= 316

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Absolute change in total sweat production assessed by GM from Baseline (Day 1b) to Week 4

End point title	3b: Secondary efficacy endpoint: Absolute change in total sweat production assessed by GM from Baseline (Day 1b) to Week 4

End point description:

Absolute change in logarithmic values of total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1b) to Week 4 in the 1% GPB group. For the long-term part of the study (Phase 3b), the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

End point type	Secondary

End point timeframe:

Baseline (Day 1b) to Week 4

End point values	1% GPB (FASnewb)			
Subject group type	Subject analysis set			
Number of subjects analysed	313			
Units: mg				
log mean (standard deviation)	-1.642 (± 2.132)			

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by GM at Week 4

End point title	3b: Secondary efficacy endpoint: Percentage of responders assessed by GM at Week 4

End point description:

Responders are defined as patients with at least 50%, 75%, and 90% sweat reduction assessd by gravimetric measurement (GM) compared to Baseline. For the long-term part of the study (Phase 3b), the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

End point type	Secondary

End point timeframe:

Week 4

End point values	1% GPB (FASnewb)			
Subject group type	Subject analysis set			
Number of subjects analysed	357			
Units: percentage of patients				
number (not applicable)				
≥50%	55.5			
≥75%	38.9			
≥90%	21.8			

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by GM at Week 12

End point title	3b: Secondary efficacy endpoint: Percentage of responders assessed by GM at Week 12

End point description:

Responders are defined as patients with at least 50%, 75%, and 90% sweat reduction assessd by gravimetric measurement (GM) compared to Baseline. For the long-term part of the study (Phase 3b), the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

End point type	Secondary

End point timeframe:

Week 12

End point values	1% GPB (FASnewb)			
Subject group type	Subject analysis set			
Number of subjects analysed	357			
Units: percentage of patients				
number (not applicable)				
≥50%	54.1			
≥75%	36.4			
≥90%	21.6			

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Weeks 4, 8, 52, and 72 (unequal 25%)

End point title	3b: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Weeks 4, 8, 52, and 72 (unequal 25%)

End point description:

Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 52, 72

End point values	1% GPB (FASb)			
Subject group type	Subject analysis set			
Number of subjects analysed	518[7]			
Units: percentage of patients				
number (not applicable)				
Week 4	20.7			
Week 8	26.6			
Week 52	30.1			
Week 72	32.0			

Notes:

[7] - Week 4: N=357 (newly recruited patients only)
Week 8: N=518
Week 52: N=518
Week 72: N=518

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Week 12 (unequal 50%)

End point title	3b: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Week 12 (unequal 50%)

End point description:

Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

End point type	Secondary

End point timeframe:

Week 12

End point values	1% GPB (FASb)	1% GPB (PPSb)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	518	326		
Units: percentage of patients				
number (not applicable)	28.0	31.6		

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Absolute change in the HDSS from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

End point title	3b: Secondary efficacy endpoint: Absolute change in the HDSS from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

End point description:

Change of the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 28, 52, and 72

End point values	1% GPB (FASb)			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: score				
median (full range (min-max))				
Week 4	-1 (-3 to 1)			
Week 8	-1 (-3 to 1)			
Week 12	-1 (-3 to 1)			
Week 28	-1 (-3 to 1)			
Week 52	-1 (-3 to 1)			
Week 72	-1 (-3 to 1)			

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Absolute change in the HidroQoL from Baseline (Day 1b) to Weeks 4, 8, 28, 52, and 72

End point title	3b: Secondary efficacy endpoint: Absolute change in the HidroQoL from Baseline (Day 1b) to Weeks 4, 8, 28, 52, and 72

End point description:

The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated.

End point type	Secondary

End point timeframe:

Baseline (Day 1 b) to Weeks 4, 8, 28, 52, and 72

End point values	1% GPB (FASb)			
Subject group type	Subject analysis set			
Number of subjects analysed	518[8]			
Units: Score				
median (full range (min-max))				
Week 4	-7.0 (-36.0 to 6.0)			
Week 8	-10.0 (-36.0 to 5.0)			
Week 28	-13.0 (-36.0 to 6.0)			
Week 52	-16.0 (-36.0 to 6.0)			
Week 72	-17.0 (-36.0 to 9.0)			

Notes:

[8] - Week 4: N=332
Week 8: N=474
Week 28: N=430
Week 52: N=383
Week 72: N=369

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HidroQoL (≥4-point improvement from Baseline (Day 1b)) at Weeks 4, 8, 12, 28, 52, and 72

End point title	3b: Secondary efficacy endpoint: Percentage of responders assessed by the HidroQoL (≥4-point improvement from Baseline (Day 1b)) at Weeks 4, 8, 12, 28, 52, and 72

End point description:

The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 28, 52, and 72

End point values	1% GPB (FASb)			
Subject group type	Subject analysis set			
Number of subjects analysed	518[9]			
Units: percent				
number (not applicable)				
Week 4	64.7			
Week 8	72.4			
Week 12	76.1			
Week 28	72.2			
Week 52	65.6			
Week 72	64.9			

Notes:

[9] - Week 4: N=357
Week 8, 12, 28, 52 and 72: N=518

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Absolute change in the DLQI questionnaire from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

End point title	3b: Secondary efficacy endpoint: Absolute change in the DLQI questionnaire from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

End point description:

The Dermatology Life Quality Index [DLQI] is scored on a 4-point scale: 'very much' = 3, 'a lot' = 2, 'a little' = 1, 'not at all' or 'question not relevant' = 0. It is calculated as sum score of all questions resulting in a total score between 0 and 30. The higher the score, the more the quality of life is impaired.

End point type	Secondary

End point timeframe:

Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

End point values	1% GPB (FASb)			
Subject group type	Subject analysis set			
Number of subjects analysed	518[10]			
Units: Score				
median (full range (min-max))				
Week 4	-6 (-30 to 13)			
Week 8	-7 (-30 to 19)			
Week 12	-7 (-30 to 21)			
Week 28	-8 (-28 to 21)			
Week 52	-9 (-28 to 12)			
Week 72	-10 (-27 to 8)			

Notes:

[10] - Week 4: N=331
Week 8: N=472
Week 12: N=468
Week 28: N=430
Week 52: N=383
Week 72: N=369

Statistical analyses

No statistical analyses for this end point

Secondary: 3b: Secondary efficacy endpoint: Absolute change in patient-rated hyperhidrosis severity from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

End point title	3b: Secondary efficacy endpoint: Absolute change in patient-rated hyperhidrosis severity from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

End point description:

The patient-rated hyperhidrosis severity was assessed by asking the following question: "How did you perceive your underarm sweating in the past 24 hours?" and is rated on a scale from 0 (no sweating at all) to 10 (worst sweating that you ever had).

End point type	Secondary

End point timeframe:

Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

End point values	1% GPB (FASb)			
Subject group type	Subject analysis set			
Number of subjects analysed	518[11]			
Units: Score				
median (full range (min-max))				
Week 4	-3 (-10 to 2)			
Week 8	-3 (-10 to 3)			
Week 12	-3 (-10 to 5)			
Week 28	-3 (-10 to 3)			
Week 52	-4 (-10 to 2)			
Week 72	-4 (-10 to 3)			

Notes:

[11] - Week 4: N=217
Week 8: N=211
Week 12: N=210
Week 28: N=189

Week 52: N=169
Week 72: N=163

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline (BL) to Week 72	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups	
Reporting group title	Phase 3a: 1% GPB (SAFa)
Reporting group description: Phase 3a: Treatment-emergent adverse events which started up to and including Day 29 or Week 4; patients self-administered the 1% GPB cream once daily in this period (SAFa, N=171)	
Reporting group title	Phase 3a: Placebo (SAFa)
Reporting group description: Phase 3a: Treatment-emergent adverse events which started up to and including Day 29 or Week 4; patients self-administered the placebo cream once daily in this period (SAFa, N=171)	
Reporting group title	Phase 3b: BL to Day 29/Week 4 - 1% GPB patients only (SAFb)
Reporting group description: Phase 3b: Treatment-emergent adverse events which started up to and including Day 29 or Week 4: Phase 3a (1% GPB only; N=81) PLUS Phase 3b (patients newly recruited to Phase 3b; N=357); patients self-administered the 1% GPB cream once daily in this period (SAFb, N=518)	
Reporting group title	Phase 3b: After Day 29/Week 4 to Week 72 (SAFb)
Reporting group description: Phase 3b: Treatment-emergent adverse events which started after Day 29 or Week 4 until Weeek 72 (EOTb): patients administered the 1% GPB cream as needed (at least twice per week and at most once daily) in this period (SAFb, N=518)	
Reporting group title	Phase 3b: BL to Week 72 - 1% GPB patients only (SAFb)
Reporting group description: Phase 3b: Treatment-emergent adverse events which started up to Week 72 (without AEs of Placebo patients during Phase 3a): all patients in the long-term part (SAFb, N=518)	
Reporting group title	Phase 3b: BL to Week 72 - 1% GPB patients only (SAF)
Reporting group description: Phase 3b: Treatment-emergent adverse events which started up to Week 72 (without AEs of Placebo patients during Phase 3a): all patients in the safety analysis set who received GPB (SAF, N=528)	

Serious adverse events	Phase 3a: 1% GPB (SAFa)	Phase 3a: Placebo (SAFa)	Phase 3b: BL to Day 29/Week 4 - 1% GPB patients only (SAFb)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	1 / 438 (0.23%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Ovarian operation			

subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Sinus operation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Gait disturbance			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Reproductive system and breast disorders			
Asthma			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Psychiatric disorders			
Chronic idiopathic pain syndrome			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Depression			

subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Injury, poisoning and procedural complications			
Electric shock			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	1 / 438 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Humerus fracture			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Congenital, familial and genetic disorders			
Micrognathia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Nervous system disorders			
Relapsing-remitting multiple sclerosis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Ear and labyrinth disorders			
Tympanic membrane perforation			

subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Eye disorders			
Mydriasis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Pupils unequal			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Scleritis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Umbilical hernia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Corona virus infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Otitis media			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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
Vestibular neuronitis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (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

Serious adverse events	Phase 3b: After Day 29/Week 4 to Week 72 (SAFb)	Phase 3b: BL to Week 72 - 1% GPB patients only (SAFb)	Phase 3b: BL to Week 72 - 1% GPB patients only (SAF)
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 518 (4.25%)	23 / 518 (4.44%)	23 / 528 (4.36%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Ovarian operation			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus operation			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			

subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Gait disturbance			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Asthma			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Tonsillar hypertrophy			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Chronic idiopathic pain syndrome			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	2 / 518 (0.39%)	2 / 518 (0.39%)	2 / 528 (0.38%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Electric shock			
subjects affected / exposed	0 / 518 (0.00%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			

subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Micrognathia			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Relapsing-remitting multiple sclerosis			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Mydriasis			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pupils unequal			

subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scleritis			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn's disease			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 518 (0.39%)	2 / 518 (0.39%)	2 / 528 (0.38%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vestibular neuronitis			
subjects affected / exposed	1 / 518 (0.19%)	1 / 518 (0.19%)	1 / 528 (0.19%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Phase 3a: 1% GPB (SAFa)	Phase 3a: Placebo (SAFa)	Phase 3b: BL to Day 29/Week 4 - 1% GPB patients only (SAFb)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 87 (49.43%)	37 / 84 (44.05%)	179 / 438 (40.87%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 87 (0.00%)	2 / 84 (2.38%)	0 / 438 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 87 (10.34%)	8 / 84 (9.52%)	28 / 438 (6.39%)
occurrences (all)	11	10	38
Migraine			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	1 / 438 (0.23%)
occurrences (all)	1	0	1
Dizziness			
subjects affected / exposed	1 / 87 (1.15%)	2 / 84 (2.38%)	1 / 438 (0.23%)
occurrences (all)	1	2	1
General disorders and administration site conditions			
Application site erythema			
subjects affected / exposed	5 / 87 (5.75%)	4 / 84 (4.76%)	13 / 438 (2.97%)
occurrences (all)	5	4	13
Application site irritation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	5 / 438 (1.14%)
occurrences (all)	0	0	5
Application site pain			
subjects affected / exposed	1 / 87 (1.15%)	1 / 84 (1.19%)	4 / 438 (0.91%)
occurrences (all)	1	1	4
Application site papules			

subjects affected / exposed	2 / 87 (2.30%)	0 / 84 (0.00%)	2 / 438 (0.46%)
occurrences (all)	3	0	3
Application site pruritus			
subjects affected / exposed	1 / 87 (1.15%)	1 / 84 (1.19%)	4 / 438 (0.91%)
occurrences (all)	3	1	7
Pyrexia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	1 / 438 (0.23%)
occurrences (all)	0	0	1
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 87 (1.15%)	1 / 84 (1.19%)	6 / 438 (1.37%)
occurrences (all)	1	1	6
Ocular hyperaemia			
subjects affected / exposed	2 / 87 (2.30%)	0 / 84 (0.00%)	2 / 438 (0.46%)
occurrences (all)	2	0	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	4 / 438 (0.91%)
occurrences (all)	1	0	5
Diarrhoea			
subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	2 / 438 (0.46%)
occurrences (all)	0	1	2
Dry mouth			
subjects affected / exposed	16 / 87 (18.39%)	4 / 84 (4.76%)	43 / 438 (9.82%)
occurrences (all)	16	4	45
Nausea			
subjects affected / exposed	0 / 87 (0.00%)	1 / 84 (1.19%)	4 / 438 (0.91%)
occurrences (all)	0	2	4
Gastritis			
subjects affected / exposed	0 / 87 (0.00%)	2 / 84 (2.38%)	0 / 438 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 87 (0.00%)	2 / 84 (2.38%)	7 / 438 (1.60%)
occurrences (all)	0	2	7
Nasal dryness			

subjects affected / exposed	2 / 87 (2.30%)	0 / 84 (0.00%)	5 / 438 (1.14%)
occurrences (all)	2	0	5
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 87 (1.15%)	0 / 84 (0.00%)	3 / 438 (0.68%)
occurrences (all)	1	0	3
Rash papular			
subjects affected / exposed	0 / 87 (0.00%)	2 / 84 (2.38%)	0 / 438 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 87 (1.15%)	1 / 84 (1.19%)	4 / 438 (0.91%)
occurrences (all)	1	2	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 87 (11.49%)	14 / 84 (16.67%)	50 / 438 (11.42%)
occurrences (all)	11	14	54
Corona virus infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 84 (0.00%)	0 / 438 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	2 / 87 (2.30%)	0 / 84 (0.00%)	2 / 438 (0.46%)
occurrences (all)	2	0	2

Non-serious adverse events	Phase 3b: After Day 29/Week 4 to Week 72 (SAFb)	Phase 3b: BL to Week 72 - 1% GPB patients only (SAFb)	Phase 3b: BL to Week 72 - 1% GPB patients only (SAF)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	346 / 518 (66.80%)	378 / 518 (72.97%)	379 / 528 (71.78%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 518 (0.58%)	3 / 518 (0.58%)	3 / 528 (0.57%)
occurrences (all)	3	3	3
Nervous system disorders			
Headache			
subjects affected / exposed	68 / 518 (13.13%)	85 / 518 (16.41%)	85 / 528 (16.10%)
occurrences (all)	168	206	206
Migraine			

subjects affected / exposed	13 / 518 (2.51%)	14 / 518 (2.70%)	14 / 528 (2.65%)
occurrences (all)	27	28	28
Dizziness			
subjects affected / exposed	1 / 518 (0.19%)	2 / 518 (0.39%)	2 / 528 (0.38%)
occurrences (all)	1	2	2
General disorders and administration site conditions			
Application site erythema			
subjects affected / exposed	34 / 518 (6.56%)	44 / 518 (8.49%)	44 / 528 (8.33%)
occurrences (all)	67	80	80
Application site irritation			
subjects affected / exposed	7 / 518 (1.35%)	11 / 518 (2.12%)	11 / 528 (2.08%)
occurrences (all)	21	26	26
Application site pain			
subjects affected / exposed	7 / 518 (1.35%)	11 / 518 (2.12%)	11 / 528 (2.08%)
occurrences (all)	19	23	23
Application site papules			
subjects affected / exposed	10 / 518 (1.93%)	12 / 518 (2.32%)	12 / 528 (2.27%)
occurrences (all)	20	23	23
Application site pruritus			
subjects affected / exposed	16 / 518 (3.09%)	19 / 518 (3.67%)	19 / 528 (3.60%)
occurrences (all)	32	39	39
Pyrexia			
subjects affected / exposed	10 / 518 (1.93%)	11 / 518 (2.12%)	11 / 528 (2.08%)
occurrences (all)	11	12	12
Eye disorders			
Dry eye			
subjects affected / exposed	19 / 518 (3.67%)	25 / 518 (4.83%)	25 / 528 (4.73%)
occurrences (all)	20	26	26
Ocular hyperaemia			
subjects affected / exposed	1 / 518 (0.19%)	3 / 518 (0.58%)	3 / 528 (0.57%)
occurrences (all)	1	3	3
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	9 / 518 (1.74%)	13 / 518 (2.51%)	13 / 528 (2.46%)
occurrences (all)	15	20	20
Diarrhoea			

subjects affected / exposed	9 / 518 (1.74%)	11 / 518 (2.12%)	11 / 528 (2.08%)
occurrences (all)	10	12	12
Dry mouth			
subjects affected / exposed	32 / 518 (6.18%)	63 / 518 (12.16%)	64 / 528 (12.12%)
occurrences (all)	54	99	100
Nausea			
subjects affected / exposed	8 / 518 (1.54%)	12 / 518 (2.32%)	12 / 528 (2.27%)
occurrences (all)	8	12	12
Gastritis			
subjects affected / exposed	9 / 518 (1.74%)	9 / 518 (1.74%)	9 / 528 (1.70%)
occurrences (all)	10	10	10
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	22 / 518 (4.25%)	29 / 518 (5.60%)	29 / 528 (5.49%)
occurrences (all)	25	32	32
Nasal dryness			
subjects affected / exposed	2 / 518 (0.39%)	7 / 518 (1.35%)	7 / 528 (1.33%)
occurrences (all)	2	7	7
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	12 / 518 (2.32%)	15 / 518 (2.90%)	15 / 528 (2.84%)
occurrences (all)	16	19	19
Rash papular			
subjects affected / exposed	0 / 518 (0.00%)	0 / 518 (0.00%)	0 / 528 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	20 / 518 (3.86%)	23 / 518 (4.44%)	23 / 528 (4.36%)
occurrences (all)	26	30	30
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	140 / 518 (27.03%)	168 / 518 (32.43%)	168 / 528 (31.82%)
occurrences (all)	202	256	256
Corona virus infection			
subjects affected / exposed	20 / 518 (3.86%)	20 / 518 (3.86%)	20 / 528 (3.79%)
occurrences (all)	20	20	20

Urinary tract infection subjects affected / exposed occurrences (all)	4 / 518 (0.77%) 6	6 / 518 (1.16%) 8	6 / 528 (1.14%) 8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 July 2019	Version 2.0 of the protocol, dated 26-Jul-2019: All changes implemented in country-specific amendments; Addition of assessment of patient-rated severity; Addition of documentation of previous hyperhidrosis treatment; Addition of option for re-screening; Update of the number of planned study centers; Clarification of anticholinergic side effects to be potentially related to the IMP; Clarification of 2 exclusion criteria (Exclusion Criteria 12 and 14); Deletion of 1 exclusion criterion (Exclusion Criterion 13); Addition of 1 exclusion criterion (Exclusion Criterion 30); Update on use of aluminum-free deodorants and recording of deodorant use in patient diary; Update of general restrictions and precautions; Update of handling of missing data; Removal of time window for Visits 3a and 3b; Change of reporting of immediately reportable events to reporting via the eCRF.
08 April 2020	Amendment 1.0 to protocol Version 2.0, dated 08-Apr-2020: Addition of a DMC to ensure the preservation of trial integrity during the time of the COVID-19 pandemic restrictions; Change in IMP dispensing during the COVID-19 pandemic; Change of some center visits to telephone visits during the COVID-19 pandemic; Temporary change of consent procedure to this amendment during the COVID 19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported