



Clinical trial results:

Efficacy and safety assessment of T4030 eye drops (unpreserved fixed combination of bimatoprost 0.01% and timolol 0.1% or 0.5%) versus Ganfort® UD (Unit Dose) in ocular hypertensive or glaucomatous patients.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2017-002823-46 |
| Trial protocol | AT PL HU BE |
| Global end of trial date | 12 February 2020 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 24 February 2021 |
| First version publication date | 24 February 2021 |
| Summary attachment (see zip file) | LT4030-201 study result summary (LT4030-201_synopsis.pdf) |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | LT4030-201 |
|-----------------------|------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Laboratoires Thea |
| Sponsor organisation address | 12 rue Blériot, Z.I. du Brézet, Clermont-Ferrand, France, 63100 |
| Public contact | Research and Development Department, Laboratoires THÉA, 33 473981436, lydia.bresson@theapharma.com |
| Scientific contact | Research and Development Department, Laboratoires THÉA, 33 473981436, lydia.bresson@theapharma.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 | 19 March 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 February 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 February 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare each combination of T4030 eye drops (unpreserved fixed combination of bimatoprost 0.01% and timolol 0.1% or 0.5%) with Ganfort® UD in terms of efficacy.

Protection of trial subjects:

Different assessments were done during subject visits in order to ensure subject safety:

- Score of each ocular symptom throughout the day (irritation/burning, stinging, itching, tearing, eye dryness feeling, foreign body sensation),
- Score of each ocular symptom upon instillation (irritation/burning, stinging, itching, tearing, eye dryness feeling, foreign body sensation),
- Score of each ocular sign (blepharitis, eyelid oedema, iris hyperpigmentation, abnormal eyelashes aspect, folliculo-papillary conjunctivitis) in each eye,
- Corneal fluorescein staining according to Oxford grading scheme in each eye,
- Far Best Corrected Visual Acuity in each eye,
- ECG,
- Clinical systemic examination (heart rate, blood pressure),
- Ocular tolerance assessed by the investigator,
- Ocular tolerance assessed by the patient,
- Ocular and systemic AE reporting.

All AEs experienced by a patient, irrespective of the suspected causality, monitored until the event has resolved, any abnormal laboratory values have returned to baseline or stabilised at a level acceptable to the investigator and Medical expert, until there is a satisfactory explanation for the changes observed, or until the patient is lost to follow-up.

Background therapy:

Patients must follow a run-in period with only brinzolamide eye drops 1% (Azopt®), one drop in each eye twice a day (morning and evening) for 5 weeks. The Azopt® treatment must be stopped 7 days before the Randomisation Visit (Day 1).

Evidence for comparator:

This study compare the efficacy, safety and pharmacokinetics of the two different formulations of unpreserved fixed combination of bimatoprost 0.01%/timolol 0.1% or 0.5% (T4030a or T4030c) to the reference product Ganfort® UD (Allergan), in OAG or OHT patients initially treated either by a combination therapy of prostaglandin and timolol (fixed or not) and controlled for at least 6 months or by a first line monotherapy for at least 6 months and insufficiently controlled.

Like for most glaucoma medications (including PGAs and -blockers eye drops), the BAK contained in the BTFC formulation has been proved to cause dose- and time-dependent toxic effects to the eye structures of the anterior segment including the tear film, cornea, conjunctiva, and even trabecular meshwork cells (Baudouin et al. 2010). Thus, the

European Medicines Agency (EMA) recommended to avoid the use of preservatives "for those patients who do not tolerate eye drops with preservatives" and "for long-term treatment", or to use, when preservatives are required, "concentration at the minimum level consistent with satisfactory antimicrobial function in each individual preparation" (EMA 2009).

Consequently, a preservative-free BTFC was developed and shown to be non-inferior in terms of efficacy compared to the preserved formulation (Goldberg et al. 2014). This preservative-free BTFC formulation is marketed since 2013 in unit dose (Ganfort® UD, Allergan)

| | |
|---|-------------------|
| Actual start date of recruitment | 28 September 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Poland: 43 |
| Country: Number of subjects enrolled | Austria: 6 |
| Country: Number of subjects enrolled | Belgium: 1 |
| Country: Number of subjects enrolled | Hungary: 36 |
| Worldwide total number of subjects | 86 |
| EEA total number of subjects | 86 |

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) | 44 |
| From 65 to 84 years | 42 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

130 patients signed informed consent. 86 subjects were randomised (+ 1 randomised by mistake) in the study in one period of 1 year.

24 participating centres in 4 countries: Austria (1), Belgium (1), Hungary (10) and Poland (12).

Recruitment started on 28SEP2018 and over on 03OCT2019.

Pre-assignment

Screening details:

Incl/excl criteria are checked at screening visit (Day -42 \pm 3). Then there is a period a run-in period (D-42 to D-7) where patient instilled Azopt wash-out period of 7 days. This period is followed by a wash-out period of 7 days. Incl/Excl criteria are confirmed at randomization visit (D1) there is a treatment period of 12 weeks.

Pre-assignment period milestones

| | |
|------------------------------|--------------------|
| Number of subjects started | 130 ^[1] |
| Number of subjects completed | 86 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|--------------------|
| Reason: Number of subjects | screen failure: 44 |
|----------------------------|--------------------|

Notes:

[1] - The number of subjects reported to have started the pre-assignment 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 reported worldwide number enrolled in the trial correspond to the the number of subjects randomized.

However, 130 subjects were screened and start pre-assignment period.

Period 1

| | |
|------------------------------|---|
| Period 1 title | treatment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind ^[2] |
| Roles blinded | Investigator, Data analyst, Assessor ^[3] |

Blinding implementation details:

Subject is not blind. It is not consider as double blind study. However assesor and data analyst are blinded.

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | T4030a |

Arm description: -

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | T4030a |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Eye gel in single-dose container |
| Routes of administration | Ocular use, Ophthalmic use |

Dosage and administration details:

patient administer the assigned treatment T4030a once daily at 20h00 (\pm 1 hour) in the conjunctival cul-de-sac of each eye.

| | |
|------------------|--------|
| Arm title | T4030c |
|------------------|--------|

Arm description: -

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|----------------------------------|
| Investigational medicinal product name | T4030c |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Eye gel in single-dose container |
| Routes of administration | Ocular use, Ophthalmic use |

Dosage and administration details:

Patient administer the assigned treatment T4030c once daily at 20h00 (\pm 1 hour) in the conjunctival cul-de-sac of each eye.

| | |
|--|--|
| Arm title | Ganfort |
| Arm description: - | |
| Arm type | Active comparator |
| Investigational medicinal product name | Ganfort® |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Eye drops, solution in single-dose container |
| Routes of administration | Ocular use, Ophthalmic use |

Dosage and administration details:

patient administer the assigned treatment Ganfort® UD once daily at 20h00 (\pm 1 hour) in the conjunctival cul-de-sac of each eye.

Notes:

[2] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.

Justification: During treatment period data analyst and assessor were also blinded in this study.

[3] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Subject is not blind. It is not consider as double blind study. However assesor and data analyst are blinded.

| Number of subjects in period 1 | T4030a | T4030c | Ganfort |
|---------------------------------------|--------|--------|---------|
| Started | 29 | 29 | 28 |
| Completed | 27 | 27 | 26 |
| Not completed | 2 | 2 | 2 |
| Adverse event, non-fatal | 2 | 2 | 2 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------|
| Reporting group title | T4030a |
| Reporting group description: - | |
| Reporting group title | T4030c |
| Reporting group description: - | |
| Reporting group title | Ganfort |
| Reporting group description: - | |

| Reporting group values | T4030a | T4030c | Ganfort |
|--|--------|--------|---------|
| Number of subjects | 29 | 29 | 28 |
| Age categorical | | | |
| The mean age is 61.6±10.9 years (range 27 to 80 years) | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 14 | 14 | 16 |
| From 65-84 years | 15 | 15 | 12 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 20 | 22 | 17 |
| Male | 9 | 7 | 11 |

| Reporting group values | Total | | |
|--|-------|--|--|
| Number of subjects | 86 | | |
| Age categorical | | | |
| The mean age is 61.6±10.9 years (range 27 to 80 years) | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 44 | | |
| From 65-84 years | 42 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 59 | | |
| Male | 27 | | |

Subject analysis sets

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | modified intent-to-treat |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

All randomised patients who received at least one dose of IMP, with at least one baseline and one post-randomisation efficacy assessment on treatment and considered as-treated (i.e., according to the treatment unit assigned at Day 1)

| Reporting group values | modified intent-to-treat | | |
|--|--------------------------|--|--|
| Number of subjects | 86 | | |
| Age categorical | | | |
| The mean age is 61.6±10.9 years (range 27 to 80 years) | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 44 | | |

| | | | |
|------------------|----|--|--|
| From 65-84 years | 42 | | |
|------------------|----|--|--|

| | | | |
|---------------------------------------|----|--|--|
| Gender categorical Units: Subjects | | | |
| Female | 59 | | |
| Male | 27 | | |

End points

End points reporting groups

| | |
|---|-----------------------------|
| Reporting group title | T4030a |
| Reporting group description: - | |
| Reporting group title | T4030c |
| Reporting group description: - | |
| Reporting group title | Ganfort |
| Reporting group description: - | |
| Subject analysis set title | modified intent-to-treat |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| All randomised patients who received at least one dose of IMP, with at least one baseline and one post-randomisation efficacy assessment on treatment and considered as-treated (i.e., according to the treatment unit assigned at Day 1) | |

Primary: Change in IOP between Day1 and Week 12 at 8h00 in the worse eye.

| | |
|--|--|
| End point title | Change in IOP between Day1 and Week 12 at 8h00 in the worse eye. |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| The Change in IOP between Day1 and Week 12 at 8h00 in the worse eye. The worse eye is defined as the eligible eye with the highest IOP at Day 1 at 8h00. In case of no IOP difference between both eyes, the right eye will be considered. | |

| End point values | T4030a | T4030c | Ganfort | modified intent-to-treat |
|---|-------------------------|--------------------------|-------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 29 | 29 | 28 | 86 |
| Units: mmHg | | | | |
| arithmetic mean (confidence interval 95%) | -9.83 (-10.66 to -9.01) | -10.14 (-11.12 to -9.15) | -9.98 (-11.12 to -8.84) | -9.98 (-11.12 to -8.84) |

Statistical analyses

| | |
|---|--------------------------|
| Statistical analysis title | Primary analysis MMRM |
| Comparison groups | T4030a v Ganfort |
| Number of subjects included in analysis | 57 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | adjusted mean difference |
| Point estimate | 1.36 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.04 |
| upper limit | 1.36 |

| | |
|---|--------------------------|
| Statistical analysis title | Primary analysis MMRM |
| Comparison groups | T4030c v Ganfort |
| Number of subjects included in analysis | 57 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | adjusted mean difference |
| Point estimate | 1.39 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.03 |
| upper limit | 1.39 |

| | |
|---|--------------------------|
| Statistical analysis title | Primary analysis MMRM |
| Comparison groups | T4030a v T4030c |
| Number of subjects included in analysis | 58 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | adjusted mean difference |
| Point estimate | 1.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.21 |
| upper limit | 1.17 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event reporting extend from start of th treatment until the final study visit.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 21.1 |

Reporting groups

| | |
|--------------------------------|---------|
| Reporting group title | T4030a |
| Reporting group description: - | |
| Reporting group title | T4030c |
| Reporting group description: - | |
| Reporting group title | Ganfort |
| Reporting group description: - | |

| Serious adverse events | T4030a | T4030c | Ganfort |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (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 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | T4030a | T4030c | Ganfort |
|---|------------------|------------------|-----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 29 (34.48%) | 10 / 29 (34.48%) | 9 / 28 (32.14%) |
| Investigations | | | |
| Abnormal sensation in eye | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 29 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 0 | 1 |
| Vital dye staining cornea present | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 1 / 29 (3.45%) 1 | 0 / 28 (0.00%) 0 |
| Blood pressure decreased subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 28 (3.57%) 1 |
| Breath sounds subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 |
| Injury, poisoning and procedural complications Documented hypersensitivity to administered product subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 28 (3.57%) 1 |
| Ankle fracture subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 29 (3.45%) 1 | 0 / 28 (0.00%) 0 |
| Wound subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 29 (0.00%) 0 | 0 / 28 (0.00%) 0 |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 29 (3.45%) 1 | 2 / 28 (7.14%) 2 |
| Vascular pain subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 29 (0.00%) 0 | 1 / 28 (3.57%) 1 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 29 (0.00%) 0 | 1 / 28 (3.57%) 1 |
| General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 29 (3.45%) 1 | 0 / 28 (0.00%) 0 |
| Pyrexia | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 1 / 29 (3.45%) 1 | 0 / 28 (0.00%) 0 |
| Eye disorders | | | |
| Blepharitis | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 29 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 2 | 0 | 1 |
| Eye irritation | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 2 / 29 (6.90%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 2 / 29 (6.90%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 2 | 1 |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Erythema of eyelid | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 1 / 29 (3.45%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Eye allergy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye pruritus | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 1 | 0 | 1 |
| Eye symptom | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 29 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 0 | 1 |
| Eyelids pruritus | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 29 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| Athralgia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 29 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 0 | 1 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 1 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 1 | 1 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 01 June 2019 | <ul style="list-style-type: none">- Adjustment of the number of patients to be screened in the study, due to higher screen failure rate than expected- Adjustment of the expected number of sites participating in the study (three additional sites in Poland and one additional site in Belgium)- Clarification of the exclusion criteria- More flexibility given to sites for the collection of the ICF- More flexibility given to sites for organising and performing the ECG- More flexibility given to site personal for management of pregnancy tests, vital signs and blood samplings- Allowing a time-window at the timepoints for blood sampling for pharmacokinetic analysis- Inclusion and specification of the risk-based monitoring approach- Minor clarification and administrative changes |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported