



Clinical trial results:

Exploratory study of the efficacy and safety of topical bimiralisib in an inflammatory and hyperproliferative skin condition

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2019-001189-14 |
| Trial protocol | FR |
| Global end of trial date | 16 March 2020 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 09 October 2020 |
| First version publication date | 09 October 2020 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | PQR309-401 |
|-----------------------|------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | PIQUR Therapeutics AG |
| Sponsor organisation address | Hochbergerstrasse 60C, Basel, Switzerland, CH-4057 |
| Public contact | Clinical Program Leader, PIQUR Therapeutics AG, info@piqur.com |
| Scientific contact | Clinical Program Leader, PIQUR Therapeutics AG, info@piqur.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 | 18 March 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 March 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 March 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of three concentrations of topical bimiralisib compared to matching vehicle and two approved topical medications (Daivobet® and Daivonex®) applied once daily to distinct 2 cm diameter treatment mini-zones on each patient.

Protection of trial subjects:

The study processes, potential benefits and any risks of participating in the study were explained to each patient. Patients were continuously monitored by the clinical investigators via regular study visits throughout the duration of the study. If the study drug needed to be stopped for safety, then the responsible investigator would continue to monitor the patient's health and determine what treatment should be given (if any) until the symptoms or findings had resolved or until a satisfactory conclusion was reached.

Background therapy:

Not applicable.

Evidence for comparator:

Two active comparators were used: Daivobet ointment and Daivonex ointment. Daivobet contains two active substances: calcipotriol and betamethasone. The vitamin D derivative, Calcipotriol, acts through receptors prevent skin proliferation that causes the scaly patches in psoriasis. Betamethasone is an anti-inflammatory that helps reduce the inflammation and itching that occur with psoriasis. Daivonex contains only calcipotriol. Both medicinal products have been approved for over 15 years for topical treatment of plaque psoriasis and have previously been used as positive comparators in the established 4-week Psoriasis Plaque Test (PPT), which formed the basis of the current study.

| | |
|---|------------------|
| Actual start date of recruitment | 12 November 2019 |
| 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 | France: 24 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 24 |

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) | 21 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from 12-Nov-2019 until 15-Jan-2020 to one clinical site in Nice, France.

Pre-assignment

Screening details:

In total 26 patients were screened, of which 24 were enrolled in the study. Two patients were not enrolled because they did not meet inclusion criteria (07 and 09, respectively).

Period 1

| | |
|------------------------------|-----------------------------------|
| Period 1 title | Treatment Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Investigator ^[1] |

Blinding implementation details:

The study was not double-blinded as the two commercially-available active comparators were distinguishable from the other IMPs. However, the study was considered investigator-blinded since IMP applications were performed out of sight of the investigator/evaluator.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | No |
| Arm title | Vehicle |

Arm description: -

| | |
|--|---------------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Vehicle (non-aqueous gel) |
| Investigational medicinal product code | N/A |
| Other name | |
| Pharmaceutical forms | Gel |
| Routes of administration | Topical use |

Dosage and administration details:

50 µL vehicle was administered once daily for six consecutive days per week for four weeks (24 applications) on a 2-cm diameter mini-zone.

| | |
|------------------|------------------------|
| Arm title | Bimiralisib 0.5% (w/w) |
|------------------|------------------------|

Arm description: -

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | bimiralisib 0.5% (w/w) gel |
| Investigational medicinal product code | PQR309 |
| Other name | |
| Pharmaceutical forms | Gel |
| Routes of administration | Topical use |

Dosage and administration details:

50 µL bimiralisib 0.5% (w/w) non-aqueous gel was administered once daily for six consecutive days per week for four weeks (24 applications) on a 2-cm diameter mini-zone.

| | |
|------------------|------------------------|
| Arm title | Bimiralisib 2.0% (w/w) |
|------------------|------------------------|

Arm description: -

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

| | |
|--|----------------------------|
| Investigational medicinal product name | bimiralisib 2.0% (w/w) gel |
| Investigational medicinal product code | PQR309 |
| Other name | |
| Pharmaceutical forms | Gel |
| Routes of administration | Topical use |

Dosage and administration details:

50 µL bimiralisib 2.0% (w/w) non-aqueous gel was administered once daily for six consecutive days per week for four weeks (24 applications) on a 2-cm diameter mini-zone.

| | |
|------------------|------------------------|
| Arm title | Bimiralisib 6.3% (w/w) |
|------------------|------------------------|

Arm description: -

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | bimiralisib 6.3% (w/w) gel |
| Investigational medicinal product code | PQR309 |
| Other name | |
| Pharmaceutical forms | Gel |
| Routes of administration | Topical use |

Dosage and administration details:

50 µL bimiralisib 6.3% (w/w) non-aqueous gel was administered once daily for six consecutive days per week for four weeks (24 applications) on a 2-cm diameter mini-zone.

| | |
|------------------|----------|
| Arm title | Daivobet |
|------------------|----------|

Arm description: -

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Daivobet ointment |
| Investigational medicinal product code | |
| Other name | Betamethasone (as dipropionate) 0.5mg/g + Calcipotriol 50µg/g |
| Pharmaceutical forms | Ointment |
| Routes of administration | Topical use |

Dosage and administration details:

50 µL Daivobet ointment (betamethasone (as dipropionate) 0.5mg/g + calcipotriol 50µg/g) was administered once daily for six consecutive days per week for four weeks (24 applications) on a 2-cm diameter mini-zone.

| | |
|------------------|----------|
| Arm title | Daivonex |
|------------------|----------|

Arm description: -

| | |
|--|---------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Daivonex ointment |
| Investigational medicinal product code | |
| Other name | Calcipotriol 50µg/g |
| Pharmaceutical forms | Ointment |
| Routes of administration | Topical use |

Dosage and administration details:

50 µL Daivonex ointment (calcipotriol 50µg/g) was administered once daily for six consecutive days per week for four weeks (24 applications) on a 2-cm diameter mini-zone.

Notes:

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

Justification: The study was designed as an investigator-blinded, within-patient randomised, intra-individual comparison of treatments. Hence each patient received all study treatments which were randomly allocated to one of six mini-zones selected on psoriasis plaques of identical severity. During the study, the patient and person dispensing IMP were instructed not to discuss study products with the investigator who performed evaluations.

| Number of subjects in period 1 | Vehicle | Bimiralisib 0.5% (w/w) | Bimiralisib 2.0% (w/w) |
|---------------------------------------|---------|---------------------------|---------------------------|
| Started | 24 | 24 | 24 |
| Completed | 24 | 24 | 24 |

| Number of subjects in period 1 | Bimiralisib 6.3% (w/w) | Daivobet | Daivonex |
|---------------------------------------|---------------------------|----------|----------|
| Started | 24 | 24 | 24 |
| Completed | 24 | 24 | 24 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Treatment Period |
|-----------------------|------------------|

Reporting group description: -

| Reporting group values | Treatment Period | Total | |
|---|------------------|-------|--|
| Number of subjects | 24 | 24 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 21 | 21 | |
| From 65-84 years | 3 | 3 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 56.5 | | |
| full range (min-max) | 32 to 79 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 7 | 7 | |
| Male | 17 | 17 | |
| Skin type | | | |
| Skin type according to Fitzpatrick's classification | | | |
| Units: Subjects | | | |
| Type II | 2 | 2 | |
| Type III | 20 | 20 | |
| Type IV | 2 | 2 | |

End points

End points reporting groups

| | |
|--------------------------------|------------------------|
| Reporting group title | Vehicle |
| Reporting group description: - | |
| Reporting group title | Bimiralisib 0.5% (w/w) |
| Reporting group description: - | |
| Reporting group title | Bimiralisib 2.0% (w/w) |
| Reporting group description: - | |
| Reporting group title | Bimiralisib 6.3% (w/w) |
| Reporting group description: - | |
| Reporting group title | Daivobet |
| Reporting group description: - | |
| Reporting group title | Daivonex |
| Reporting group description: - | |

Primary: AUEC of Total Clinical Score

| | |
|------------------------|---|
| End point title | AUEC of Total Clinical Score |
| End point description: | The primary efficacy endpoint was the Area Under the Effect Curve (AUEC) of Total Clinical Score (TCS) calculated from Day 1 to Day 29 using the trapezoidal rule. The lower the AUEC1-29, the stronger is the activity of the drug. TCS was defined in the protocol as the sum of psoriasis severity index scores of erythema, scaling and induration. |
| End point type | Primary |
| End point timeframe: | |
| From Day 1 to Day 29 | |

| End point values | Vehicle | Bimiralisib 0.5% (w/w) | Bimiralisib 2.0% (w/w) | Bimiralisib 6.3% (w/w) |
|--------------------------------------|------------------|------------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 24 | 24 | 24 | 24 |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | 170.69 (± 33.51) | 157.65 (± 44.04) | 160.92 (± 31.46) | 171.31 (± 37.66) |

| End point values | Daivobet | Daivonex | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 24 | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | 58.31 (± 19.00) | 92.52 (± 27.05) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Analysis of AUEC1-29 of the TCS |
| Statistical analysis description: The AUEC1-29 of the TCS was analyzed using a mixed-effect model. This model included treatment as fixed effect and subject as random effect. The treatments were compared using the Tukey Kramer multiple comparison test performed at a 5% two-sided significance level. | |
| Comparison groups | Vehicle v Bimimalisib 0.5% (w/w) v Bimimalisib 2.0% (w/w) v Bimimalisib 6.3% (w/w) v Daivobet v Daivonex |
| Number of subjects included in analysis | 144 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | ≤ 0.05 |
| Method | Mixed models analysis |
| Parameter estimate | Mean difference (final values) |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| Variability estimate | Standard deviation |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The analysis of adverse events (AEs) is based on treatment emergent adverse events (TEAEs), defined as all AEs occurring or worsening after first dose of IMP.

Adverse event reporting additional description:

Safety assessments were conducted for all patients at the screening visit (following ICF signature) and at every subsequent visit. Safety parameters were: 1) Local tolerance assessed twice weekly using a 4-point scale for each mini-zone, and 2) Monitoring and recording of AEs.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Safety Population |
|-----------------------|-------------------|

Reporting group description:

All randomized patients who received at least one dose of the study products (i.e. either test or reference products).

| Serious adverse events | Safety Population | | |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 24 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | Safety Population | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 24 (16.67%) | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 24 (8.33%) | | |
| occurrences (all) | 2 | | |
| Infections and infestations | | | |

| | | | |
|-----------------------------|----------------|--|--|
| Paronychia | | | |
| subjects affected / exposed | 1 / 24 (4.17%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| This study involved an intra-individual comparison of treatments therefore each patient received each of the five IMPs randomized to five treatment mini-zones. The total number of patients in the analysis was thus 24 (and not 144). |
|---|

Notes: