# Clinical trial results:
# A phase IIa randomized, active-controlled, double-blind, dose-escalation study in patients with vulvovaginal candidiasis to evaluate clinical efficacy, safety and tolerability and dose response relationship of topically administered ProF-001

## Summary

| | |
|---|---|
| EudraCT number | 2016-004268-21 |
| Trial protocol | AT |
| Global end of trial date | 30 July 2018 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 01 August 2020 |
| First version publication date | 01 August 2020 |
| Summary attachment (see zip file) | Prof-001_Public disclosure synopsis_Version 1.1 (Prof-001_Public disclosure synopsis_Version 1.1.pdf) |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | ProF-001_Phase_IIa |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03115073 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Profem GmbH |
| Sponsor organisation address | Riglergasse 4/I, Vienna, Austria, 1180 |
| Public contact | Sponsor representative, Profem GmbH<br>DDr. Marion Noe-Letschnig<br>E-mail: marion.noe@profem.at<br>, +43 676 7203070, office@profem.at |
| Scientific contact | Sponsor representative, Profem GmbH<br>DDr. Marion Noe-Letschnig<br>E-mail: marion.noe@profem.at<br>, +43 676 7203070, office@profem.at |

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 | 20 November 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 July 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 July 2018 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To determine the dose-response and the clinical efficacy of a cream containing a combination of clotrimazole and diclofenac sodium for the topical treatment of acute episodes of vulvovaginal candidiasis (VVC) after vaginal administration. Three different doses of diclofenac sodium in combination with clotrimazole were compared with clotrimazole alone as reference.

Protection of trial subjects:

Adverse event monitoring included subjective and objective symptom assessments applying an established symptom score as defined in the FDA guidance for treatment of VVC from 2016 and by Sobel and co-workers in 2001:

- Subjective symptoms: itching, burning pain and irritation/soreness classified as mild, moderate and severe,
- Objective symptoms: erythma, edema and excoriation as assessed by the gynecologist (classified as mild, moderate and severe).

Study subjects were asked to self-rate their physical condition and adverse reactions associated with the study medication at each visit. Subjective grading of local reactions has been documented by patients in the diary according to severity based on a visual analogue scale (VAS). The treating physician assessed the symptoms itching, burning pain and irritation/soreness according to the above mentioned symptom score (categorized into mild, moderate and severe) and objectively confirmed by gynecological examination.
Special attention of participating subjects has been drawn to document in the diary and to report the occurrence of local irritations such as erythema, peeling, itching or burning.

Background therapy:

not applicable

Evidence for comparator:

1% Clotrimazole for acute episode of VVC (015-072l_S2k_Vulvovaginalkandidose_2013-12; Pappas et al. US_clinical_practice_guideline_2016)

| | |
|---|---|
| Actual start date of recruitment | 09 May 2017 |
| 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 | Austria: 54 |
| Country: Number of subjects enrolled | Poland: 32 |
| 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) | 86 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Recruitment was performed at secondary and tertiary care gynecology units in Austria (Vienna and Tyrolia) and Poland (City of Poznan).

### Pre-assignment

Screening details:

Subject screening and entry examination included but was not limited to the grading of signs and symptoms by a gynaecologist and the performance of a vaginal smear (native, KOH) for budding yeasts and/or fungal (pseudo-)hyphae, normal (G I) or intermediate flora (G II) according to the Nugent criteria for the diagnosis of an acute episode of VVC.

### Period 1

| | |
|---|---|
| Period 1 title | Active treatment period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Monitor, Subject, Data analyst, Carer, Assessor |

Blinding implementation details:

Central blinding of IMP was performed at manufacturing site - blinding was kept throughout the study until database lock

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Control |

Arm description:

Active controlled arm with Clotrimazole 1%

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | clotrimazole 1% |
| Investigational medicinal product code | comparator |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Vaginal use |

Dosage and administration details:

cream containing 1% clotrimazole (Fungizid-ratiopharm® 1% Vaginalcreme) for intravaginal application (2.5 ml cream) and topical application (2 cm cream in the vulvar region)

| | |
|---|---|
| **Arm title** | Candiplus 0.2% |

Arm description:

Lowest dose group

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Candiplus 0.2% |
| Investigational medicinal product code | clotrimazole 1% + diclofenac 0.2% |
| Other name | ProF-001 0.2% |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use , Vaginal use |

Dosage and administration details:

2.5 ml + 2 cm cream twice daily (days 1, 2 and 3) followed by 2.5 ml + 2 cm cream once daily (days 4, 5 and 6) to be administered as vaginal application (2.5 ml cream) and topical application (2 cm cream in the vulvar region)

| | |
|---|---|
| **Arm title** | Candiplus 0.3% |

Arm description:

Intermediate dose group

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Candiplus 0.3% |
| Investigational medicinal product code | clotrimazole 1% + diclofenac 0.3% |
| Other name | ProF-001 0.3% |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use , Vaginal use |

Dosage and administration details:

2.5 ml + 2 cm cream twice daily (days 1, 2 and 3) followed by 2.5 ml + 2 cm cream once daily (days 4, 5 and 6) to be administered as vaginal application (2.5 ml cream) and topical application (2 cm cream in the vulvar region)

| | |
|---|---|
| **Arm title** | Candiplus 0.4% |

Arm description:

High dose group

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Candiplus 0.4% |
| Investigational medicinal product code | clotrimazole 1% + diclofenac 0.4% |
| Other name | ProF-001 0.4% |
| Pharmaceutical forms | Cream |
| Routes of administration | Vaginal use, Topical use |

Dosage and administration details:

2.5 ml + 2 cm cream twice daily (days 1, 2 and 3) followed by 2.5 ml + 2 cm cream once daily (days 4, 5 and 6) to be administered as vaginal application (2.5 ml cream) and topical application (2 cm cream in the vulvar region)

| **Number of subjects in period 1** | Control | Candiplus 0.2% | Candiplus 0.3% |
|---|---|---|---|
| Started | 21 | 22 | 21 |
| Completed | 20 | 21 | 21 |
| Not completed | 1 | 1 | 0 |
| Protocol deviation | 1 | 1 | - |

| **Number of subjects in period 1** | Candiplus 0.4% |
|---|---|
| Started | 22 |
| Completed | 21 |
| Not completed | 1 |
| Protocol deviation | 1 |

## Period 2

| | |
|---|---|
| Period 2 title | Follow up period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Control |

Arm description:

Active controlled arm with Clotrimazole 1%

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | clotrimazole 1% |
| Investigational medicinal product code | comparator |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Vaginal use |

Dosage and administration details:

cream containing 1% clotrimazole (Fungizid-ratiopharm® 1% Vaginalcreme) for intravaginal application (2.5 ml cream) and topical application (2 cm cream in the vulvar region)

| | |
|---|---|
| **Arm title** | Candiplus 0.2% |

Arm description:

Lowest dose group

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Candiplus 0.2% |
| Investigational medicinal product code | clotrimazole 1% + diclofenac 0.2% |
| Other name | ProF-001 0.2% |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use , Vaginal use |

Dosage and administration details:

2.5 ml + 2 cm cream twice daily (days 1, 2 and 3) followed by 2.5 ml + 2 cm cream once daily (days 4, 5 and 6) to be administered as vaginal application (2.5 ml cream) and topical application (2 cm cream in the vulvar region)

| | |
|---|---|
| **Arm title** | Candiplus 0.3% |

Arm description:

Intermediate dose group

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Candiplus 0.3% |
| Investigational medicinal product code | clotrimazole 1% + diclofenac 0.3% |
| Other name | ProF-001 0.3% |
| Pharmaceutical forms | Cream |
| Routes of administration | Topical use , Vaginal use |

Dosage and administration details:

2.5 ml + 2 cm cream twice daily (days 1, 2 and 3) followed by 2.5 ml + 2 cm cream once daily (days 4, 5 and 6) to be administered as vaginal application (2.5 ml cream) and topical application (2 cm cream in the vulvar region)

| | |
|---|---|
| **Arm title** | Candiplus 0.4% |

Arm description:

High dose group

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Candiplus 0.4% |
| Investigational medicinal product code | clotrimazole 1% + diclofenac 0.4% |
| Other name | ProF-001 0.4% |
| Pharmaceutical forms | Cream |
| Routes of administration | Vaginal use, Topical use |

Dosage and administration details:

2.5 ml + 2 cm cream twice daily (days 1, 2 and 3) followed by 2.5 ml + 2 cm cream once daily (days 4, 5 and 6) to be administered as vaginal application (2.5 ml cream) and topical application (2 cm cream in

the vulvar region)

| **Number of subjects in period 2** | Control | Candiplus 0.2% | Candiplus 0.3% |
|---|---|---|---|
| Started | 20 | 21 | 21 |
| Completed | 20 | 21 | 21 |

| **Number of subjects in period 2** | Candiplus 0.4% |
|---|---|
| Started | 21 |
| Completed | 21 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Control |
| Reporting group description: | |
| Active controlled arm with Clotrimazole 1% | |
| Reporting group title | Candiplus 0.2% |
| Reporting group description: | |
| Lowest dose group | |
| Reporting group title | Candiplus 0.3% |
| Reporting group description: | |
| Intermediate dose group | |
| Reporting group title | Candiplus 0.4% |
| Reporting group description: | |
| High dose group | |

| Reporting group values | Control | Candiplus 0.2% | Candiplus 0.3% |
|---|---|---|---|
| Number of subjects | 21 | 22 | 21 |
| 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) | 21 | 22 | 21 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| median | 28 | 26 | 34 |
| full range (min-max) | 19 to 41 | 18 to 45 | 18 to 45 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 21 | 22 | 21 |
| Male | 0 | 0 | 0 |

| Reporting group values | Candiplus 0.4% | Total | |
|---|---|---|---|
| Number of subjects | 22 | 86 | |
| 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) | 22 | 86 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 32 | | |
| full range (min-max) | 18 to 48 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 22 | 86 | |
| Male | 0 | 0 | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Full analysis set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The full analysis set will comprise all randomized subjects who received at least six doses (3 days) of investigational product and who have sufficient data of the co-efficacy endpoint of: (i) Symptom relief within the first 60 minutes (after application of investigational product or active control, with reduction of the subjective symptom score ≥2) and (ii) clinical cure (absence of signs and symptoms of VVC) at the TOC visit (=day 7 ± 3). Analyses on the FAS will be performed according to the randomized dose group (intention to treat principle).

| | |
|---|---|
| Subject analysis set title | Safety population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The safety population comprises all subjects who were randomized and received at least one dose of the IMP. Analyses based on the safety analyses were performed according to the actual dose the patients received.

| **Reporting group values** | Full analysis set | Safety population | |
|---|---|---|---|
| Number of subjects | 83 | 86 | |
| 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) | 83 | 86 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 29 | 29 | |
| full range (min-max) | 18 to 48 | 18 to 48 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |

| | | | |
|---|---|---|---|
| Male | | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Control |
| Reporting group description: | |
| Active controlled arm with Clotrimazole 1% | |
| Reporting group title | Candiplus 0.2% |
| Reporting group description: | |
| Lowest dose group | |
| Reporting group title | Candiplus 0.3% |
| Reporting group description: | |
| Intermediate dose group | |
| Reporting group title | Candiplus 0.4% |
| Reporting group description: | |
| High dose group | |
| Reporting group title | Control |
| Reporting group description: | |
| Active controlled arm with Clotrimazole 1% | |
| Reporting group title | Candiplus 0.2% |
| Reporting group description: | |
| Lowest dose group | |
| Reporting group title | Candiplus 0.3% |
| Reporting group description: | |
| Intermediate dose group | |
| Reporting group title | Candiplus 0.4% |
| Reporting group description: | |
| High dose group | |
| Subject analysis set title | Full analysis set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The full analysis set will comprise all randomized subjects who received at least six doses (3 days) of investigational product and who have sufficient data of the co-efficacy endpoint of: (i) Symptom relief within the first 60 minutes (after application of investigational product or active control, with reduction of the subjective symptom score ≥2) and (ii) clinical cure (absence of signs and symptoms of VVC) at the TOC visit (=day 7 ± 3). Analyses on the FAS will be performed according to the randomized dose group (intention to treat principle).

| | |
|---|---|
| Subject analysis set title | Safety population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

The safety population comprises all subjects who were randomized and received at least one dose of the IMP. Analyses based on the safety analyses were performed according to the actual dose the patients received.

### Primary: Symptom relief after 60 minutes with clinical cure at day 7

| | |
|---|---|
| End point title | Symptom relief after 60 minutes with clinical cure at day 7 |

End point description:

Composite primary endpoint combining two parameters:
1. Symptom relief within the first 60 minutes after application of the investigational medicinal product (IMP) defined as reduction of the subjective symptom score ≥2 in combination with
2. Clinical cure (absence of signs and symptoms of VVC) at the test of cure (TOC) visit at day 7 (±3 days)

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Symptom assessment 60 minutes after application of IMP in combination with cure at the test of cure (TOC) visit at day 7 (±3 days)

| **End point values** | Control | Candiplus 0.2% | Candiplus 0.3% | Candiplus 0.4% |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 21 | 21 | 21 |
| Units: numbers | 7 | 12 | 7 | 6 |

| **End point values** | Full analysis set | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 83 | | | |
| Units: numbers | 33 | | | |

**Statistical analyses**

| **Statistical analysis title** | logistic regression |
|---|---|

Statistical analysis description:

The logistic regression was performed to test effects of dose-concentration on the primary endpoint. Results indicated that the model did not provide a statistically significant effect (p=0.39). The Nagelkerke R2 indicated that model accounted for 1.3% of the total variance. The correct prediction rate was about 66.2%. The wald test showed that the predictor did not significantly predict the primary endpoint.

| | |
|---|---|
| Comparison groups | Control v Candiplus 0.2% v Candiplus 0.3% v Candiplus 0.4% v Full analysis set |
| Number of subjects included in analysis | 166 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | Regression, Logistic |
| Parameter estimate | regression coefficient |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Day of randomization until end of follow-up period (day 60 ± 5 days after randomization) | |
| Assessment type | Systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 21.1 |
| **Reporting groups** | |
| Reporting group title | Control |
| Reporting group description: Active controlled arm with Clotrimazole 1% | |
| Reporting group title | Candiplus 0.2% |
| Reporting group description: Lowest dose group | |
| Reporting group title | Candiplus 0.3% |
| Reporting group description: Intermediate dose group | |
| Reporting group title | Candiplus 0.4% |
| Reporting group description: High dose group | |

| Serious adverse events | Control | Candiplus 0.2% | Candiplus 0.3% |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 22 (0.00%) | 0 / 21 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

| Serious adverse events | Candiplus 0.4% | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| **Non-serious adverse events** | Control | Candiplus 0.2% | Candiplus 0.3% |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 21 (57.14%) | 12 / 22 (54.55%) | 15 / 21 (71.43%) |
| Nervous system disorders | | | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 1 / 22 (4.55%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 9 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | 1 / 22 (4.55%) | 3 / 21 (14.29%) |
| occurrences (all) | 3 | 1 | 6 |
| Reproductive system and breast disorders | | | |
| Vulvovaginal burning sensation | | | |
| subjects affected / exposed | 9 / 21 (42.86%) | 7 / 22 (31.82%) | 10 / 21 (47.62%) |
| occurrences (all) | 23 | 26 | 49 |
| Vulvovaginal disorder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 3 / 22 (13.64%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 6 | 1 |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | 2 / 22 (9.09%) | 2 / 21 (9.52%) |
| occurrences (all) | 4 | 2 | 4 |
| Genital burning sensation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 22 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 9 |
| Pruritus genital | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | 0 / 22 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 9 |

| **Non-serious adverse events** | Candiplus 0.4% | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 15 / 22 (68.18%) | | |
| Nervous system disorders | | | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | | |
| occurrences (all) | 2 | | |
| Reproductive system and breast disorders | | | |
| Vulvovaginal burning sensation | | | |
| subjects affected / exposed | 14 / 22 (63.64%) | | |
| occurrences (all) | 74 | | |
| Vulvovaginal disorder | | | |
| subjects affected / exposed | 1 / 22 (4.55%) | | |
| occurrences (all) | 1 | | |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 4 / 22 (18.18%) | | |
| occurrences (all) | 13 | | |
| Genital burning sensation | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus genital | | | |
| subjects affected / exposed | 0 / 22 (0.00%) | | |
| occurrences (all) | 0 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 05 March 2018 | Follow-up period of the last cohort amended to complete the end of trial information: The study was considered completed when the TOC visit of the last randomized patient is reached (last randomized subject completes test of cure visit) or the study is terminated early based on recommendation of the Independent Safety Monitoring Committee. Those patients who have entered the follow-up period before approval of protocol amendment V4.0 dated March 5, 2018, were to be followed up to the second telephone visit. All other patients were to be followed until the TOC visit. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported