



Clinical trial results: Chlorhexidine gluconate as treatment and prophylaxis of vulvovaginal Candidiasis

Summary

EudraCT number	2020-000758-81
Trial protocol	SE
Global end of trial date	27 November 2024

Results information

Result version number	v1 (current)
This version publication date	07 November 2025
First version publication date	07 November 2025

Trial information

Trial identification

Sponsor protocol code	Chlorhex-KKDS-2021
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05059145
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Karolinska Institutet
Sponsor organisation address	Nobels väg 6, Solna, Sweden, 17177
Public contact	Nina Bohm-Starke, Karolinska Institutet, Danderyd Hospital. Div of Obstetrics and Gynecology, +46 812355000, nina.bohm-starke@ki.se
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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 June 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2024
Global end of trial reached?	Yes
Global end of trial date	27 November 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To analyze if daily vaginal application of 8 ml of Hibitane® for one week and thereafter once a week for another 11 consecutive weeks is at least as effective as fluconazole 150 mg capsules every third day for the first three doses and thereafter 150 mg once a week for another 11 consecutive weeks regarding treatment- and prophylactic efficacy for recurrent vulvovaginal Candida albicans infection.

Protection of trial subjects:

The first ethical approval on the clinical trial was granted by the Swedish Ethical Review Authority on September 8, 2020 (Dnr 2020-04035) and the second application including more advanced molecular analyses was granted on February 6, 2022 (Dnr 2021-06538-02). All participants provided written informed consent prior to enrollment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2022
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	Sweden: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	23
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Recruitment (began April 27, 2022) was conducted via advertisements at regional gynecological clinics and on social media, inviting women with RVVC to contact the research midwife at the Women's Department at Danderyd Hospital for further information. Women meeting the age and symptom criteria were invited to a screening visit.

Pre-assignment

Screening details:

Inclusion criteria: women aged 18-50y with a history of RVVC (≥ 3 episodes of Candida infection in the past year); current symptoms consistent with acute vulvovaginal candidiasis; culture-confirmed C. albicans susceptible to FLZ.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Chlorhexidine gluconate (Hibitane®)

Arm description:

The CHG group received Hibitane® 1% vaginal cream, 7.5 mL nightly for 7 days as acute treatment, followed by prophylactic treatment with 7.5 mL once weekly for 11 consecutive weeks.

Arm type	Experimental
Investigational medicinal product name	Hibitane
Investigational medicinal product code	SUB01215MIG
Other name	CHLORHEXIDINE GLUCONATE
Pharmaceutical forms	Vaginal cream
Routes of administration	Vaginal use

Dosage and administration details:

Daily vaginal application of 8 ml of Hibitane® for one week and thereafter once a week for another 11 consecutive weeks.

Arm title	Fluconazole®
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Arm description:

The FLZ group received oral capsules Fluconazole® 150 mg every third day for the first three doses (acute phase), followed by 150 mg once weekly for 11 consecutive weeks (prophylactic phase).

Arm type	Active comparator
Investigational medicinal product name	Fluconazole
Investigational medicinal product code	SUB07674MIG
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Fluconazole 150 mg capsules every third day for the first three doses and thereafter 150 mg once a week for another 11 consecutive weeks.

Number of subjects in period 1	Chlorhexidine gluconate (Hibitane®)	Fluconazole®
Started	12	11
Completed	5	11
Not completed	7	0
Adverse event, non-fatal	7	-

Baseline characteristics

Reporting groups

Reporting group title	Chlorhexidine gluconate (Hibitane®)
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Reporting group description:

The CHG group received Hibitane® 1% vaginal cream, 7.5 mL nightly for 7 days as acute treatment, followed by prophylactic treatment with 7.5 mL once weekly for 11 consecutive weeks.

Reporting group title	Fluconazole®
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Reporting group description:

The FLZ group received oral capsules Fluconazole® 150 mg every third day for the first three doses (acute phase), followed by 150 mg once weekly for 11 consecutive weeks (prophylactic phase).

Reporting group values	Chlorhexidine gluconate (Hibitane®)	Fluconazole®	Total
Number of subjects	12	11	23
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	33	32	
full range (min-max)	24 to 46	23 to 45	-
Gender categorical Units: Subjects			
Female	12	11	23
Male	0	0	0

End points

End points reporting groups

Reporting group title	Chlorhexidine gluconate (Hibitane®)
Reporting group description: The CHG group received Hibitane® 1% vaginal cream, 7.5 mL nightly for 7 days as acute treatment, followed by prophylactic treatment with 7.5 mL once weekly for 11 consecutive weeks.	
Reporting group title	Fluconazole®
Reporting group description: The FLZ group received oral capsules Fluconazole® 150 mg every third day for the first three doses (acute phase), followed by 150 mg once weekly for 11 consecutive weeks (prophylactic phase).	
Subject analysis set title	Chlorhexidine gluconate (Hibitane®) after 1 week
Subject analysis set type	Full analysis
Subject analysis set description: 7 participants in the CHG group chose to withdraw from the study due to local pain and discomfort, and did not attend the planned visits at 3 months (end of prophylactic treatment) and 6 months (follow-up visit). Therefore, this primary result will only present end points for the first follow-up 1 week after acute treatment where we have results from all 11 in the CHG-group.	

Primary: The proportion of women in each group that has cleared the infection after 1week of treatment

End point title	The proportion of women in each group that has cleared the infection after 1week of treatment ^[1]
End point description: The early termination of the study with less than 50% of the planned number of participants (30+30 in each study arm) has impact on the interpretation of the results. However, the primary outcome of negative candida cultures after one week of treatment for an acute episode of vulvovaginal candidiasis showed an equal response in both study groups. This preliminary result indicates that chlorhexidine could be an effective alternative treatment for recurrent vulvovaginal candidiasis, but the drug in this study (Hibitane®) cannot be used, which will be the preliminary conclusion of the study.	
End point type	Primary
End point timeframe: The proportion of women in each group that has cleared the infection after 1week of treatment, defined as negative cultures for Candida albicans.	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: It was planned follow-up visits at 1 week, 3 months and 6 months. But 7 participants in CHG-group withdrew after 1 week of treatment due to adverse events, therefore we cannot report from the 3 and 6 months visits. We chose to only report from the first 1 week visit where all the CHG-group attended. However, it is important to present the withdrawal due to adverse events, hence we showed the planned baseline period arm "Chlorhexidine gluconate (Hibitane®)" but cannot do a full report.

End point values	Fluconazole®	Chlorhexidine gluconate (Hibitane®) after 1 week		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	11	12		
Units: Number of patients	12	9		

Statistical analyses

Statistical analysis title	The proportion that has cleared infection
Comparison groups	Fluconazole® v Chlorhexidine gluconate (Hibitane®) after 1 week
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.82
Method	Fisher exact

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurred within the acute treatment period (first week of treatment), or during the prophylactic treatment period between week 2 to 3 months after study start.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	n/a
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Dictionary version	n/a
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Reporting groups

Reporting group title	Fluconazole®
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Reporting group description: -	
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Reporting group title	Chlorhexidine gluconate (Hibitane®)
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Reporting group description: -	
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Serious adverse events	Fluconazole®	Chlorhexidine gluconate (Hibitane®)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Fluconazole®	Chlorhexidine gluconate (Hibitane®)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	8 / 12 (66.67%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			

subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0	
Reproductive system and breast disorders			
Pain	Additional description: Local symptoms of pain, discomfort and irritation of the vulva and vagina after the vaginal application of the study drug.		
subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	8 / 12 (66.67%) 8	
Discomfort	Additional description: Local symptoms of pain, discomfort and irritation of the vulva and vagina after the vaginal application of the study drug.		
subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	8 / 12 (66.67%) 8	
Irritability	Additional description: Local symptoms of pain, discomfort and irritation of the vulva and vagina after the vaginal application of the study drug.		
subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0	8 / 12 (66.67%) 8	

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.

The early termination of the study with less than 50% of the planned number of participants (30+30 in each study arm) has impact on the interpretation of the results.
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Notes: