ISRCTN11009040 https://doi.org/10.1186/ISRCTN11009040

Efficacy and safety of intravaginal application of "SAM vaginal gel" on suspicious cervical smear results and on CIN 1 and CIN 2 lesions

Submission date
05/12/2019

Recruitment status
No longer recruiting

Registration date
10/12/2019

Overall study status
Completed

Last Edited
28/06/2023

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Cervical dysplasia is a precancerous condition in which abnormal cell growth occurs on the surface of the cervix or endocervical canal, the opening between the uterus and the vagina. This condition is also called cervical intraepithelial neoplasia (CIN). There is no valid non-surgical treatment for mild to moderate CIN. The treatment for mild to moderate CIN (called CIN 1 and CIN 2) initially consists of close monitoring without surgical intervention. According to the literature CIN 1 and also CIN 2 show high rates of spontaneous improvements. Improvement rates and time frames for improvement are described as very heterogeneous. Therefore regular check-ups are generally agreed with the patient. There are a lot of patients who suffer from high psychological stress during this interval. The vaginal gel “SAM”, a medical device, is intended to be used during the treatment-free period until the next check-up. The aim of this study is to assess the effects on cervical dysplasia of application of the vaginal gel compared with a control group who do not get any treatment.

Who can participate?
Women between 18 and 60 years with diagnosis of cervical dysplasia (CIN1 or CIN 2)

What does the study involve?
Participants are randomly allocated to either the vaginal gel group or to the control group. Patients in the vaginal gel group receive three 28-day packages of vaginal gel on visit 1. The vaginal gel has to be applied intravaginally once a day (5 ml), except on menstruation days. For non-menstruating women, a 3-day treatment-free period is respected after 28 days of application. The control group receive no intervention according to gynaecological guidelines.

What are the possible benefits and risks of participating?
Participants may benefit from improvement in cervical dysplasia. It is expected that higher rates of improvement will occur in the vaginal gel group compared to the watch and wait group. Only a few and mild side effects like itching and burning are expected based on previous experience from using the vaginal gel.

Where is the study run from?
Three study centres in Czech Republic

When is the study starting and how long is it expected to run for?
September 2016 to January 2019

Who is funding the study?
Deflamed International s.r.o. Prague (Czech Republic)

Who is the main contact?
Mrs Gertrude Markolin
gertrude.markolin@nutropia.at

Contact information

Type(s)
Public

Contact name
Mrs Gertrude Markolin

Contact details
Moosham 29
Unternberg
Austria
5585
+43 (0)6476 805549
gertrude.markolin@nutropia.at

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
SAM-001

Study information

Scientific Title
Randomised, prospective, open-label with control group clinical trial to investigate the efficacy and safety of the topical (intravaginal) application of the gel “SAM vaginal gel” (class IIa medical device) through the regression rate of cervical smears ASC US, ASC H, LSIL, and HSIL and cervical lesions CIN 1 and CIN 2 and through the regression of the marker p16

Acronym
PMCF

Study objectives
In accordance with the state of the art in evidence-based medicine, there is no valid non-surgical therapeutic approach for mild to moderate cervical intraepithelial neoplasia (CIN). The therapy regime for CIN 1 and CIN 2 also initially consists of close monitoring without surgical intervention. According to the literature, CIN 1 and also CIN 2 show high rates of spontaneous regression. The reported percentage of regressions and time frames for regression are very heterogeneous. Therefore, regular controls are generally agreed upon with the patient, which can result in a certain level of uncertainty and anxiety for the patients concerned. A number of patients may suffer from high psychological stress during this therapy free interval. The vaginal gel “SAM” described in this study is intended to be used during the therapy free period until the next control. It is assumed that application of the vaginal gel is able to increase the number of cytological and histological regressions and to alleviate the stress of the waiting period (evaluation of stress reduction is however not the aim of the present study). Therefore, it is acceptable for medical and ethical reasons to offer the patients concerned a therapeutic approach in addition to the simple clinical control period. Preliminary data justify the planning and implementation of a clinical trial with the vaginal gel.

Null hypothesis (H0): Regression rate in SAM is lower than or equal to that in “wait and watch” group.
Alternative hypothesis (H1): Regression rate in SAM is greater than that in “wait and watch” group.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Multicentric Ethics Committee (MEC): Approved 13/02/2017, Multi-Centric Ethics Committee of Faculty Hospital Olomouc and Medical
Faculty of University Purkyně in Olomouc (Etická komise Fakultní nemocnice Olomouc a Lékařské fakulty UP v Olomouci, I.P. Pavlova 6, 775 20 Olomouc, Czech Republic; Tel: +420 (0)588 443 381; Email: Vladko.horcicka@fnol.cz), ref: 9/17 MEK 1
2. Local Ethics Committee: Approved 11/10/2017,Ethics Committee of the University Hospital Motol (Etická komise Fakultní nemocnice v Motole, 150 06 Praha 5, V uvalu 84, Czech Republic; Tel: +420 (0)224 431; Email: etickakomise@fnmotol.cz), ref: 1278/17
3. Change Sponsor Address: Approved 09/04/2018, Multi-Centric Ethics Committee of Faculty Hospital Olomouc and Medical Faculty of University Purkyně in Olomouc (Etická komise Fakultní nemocnice Olomouc a Lékařské fakulty UP v Olomouci, I.P. Pavlova 6, 775 20 Olomouc, Czech Republic; Tel: +420 (0)588 443 381; Email: Vladko.horcicka@fnol.cz), ref: 9/17 MEK 1
4. Protocol amendment (SA 9.4.2018): Approved 10/12/2018, Multi-Centric Ethics Committee of Faculty Hospital Olomouc and Medical
Faculty of University Purkyně in Olomouc (Etická komise Fakultní nemocnice Olomouc a Lékařské fakulty UP v Olomouci, I.P. Pavlova 6, 775 20 Olomouc, Czech Republic; Tel: +420 (0)588 443 381; Email: vladko.horcicka@fnol.cz), ref: 9/17 MEK 1

Study design
Randomised prospective open-label with control group multicentre study

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Cervical intraepithelial neoplasia

Interventions
Patients will be randomised to either the active arm (vaginal gel group), or to the control arm (wait and watch). Patients in the active arm will receive 3 x 28-days package of vaginal gel on visit 1. The vaginal gel has to be applied intravaginally once a day (5 ml), except on menstruation days. For non-menstruating women, a 3-day treatment-free period shall be respected after 28 days of application. The control arm will get no intervention according to gynaecological guidelines.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
DeflaGyn® Vaginal Gel

Primary outcome measure
The clinically relevant primary endpoint was the regression rate comparison after three months of follow-up between patient groups using SAM vaginal gel (DeflaGyn®) and “watch and wait” patient (control group), where the regression rate was defined as the combined endpoint of cytology and histology. Success was regarded as either cytological regression, defined as an initial ASC-US, LSIL, ASC-H or HSIL disappeared or changed to lower level (e.g. LSIL to ASC-US etc.) after treatment OR histological regression; defined as an initial CIN 1 lesion disappeared after treatment, or as an initial CIN 2 lesion replaced by CIN 1 lesion or disappeared after treatment, respectively.

Secondary outcome measures
1. Cytological regression or remission according to Bethesda, in decreasing association with squamous precancerous disease: ASC-US, AGC, LSIL, ASC-H, HSIL, after 3 and 6 months of follow-up. Remission was defined as a complete recovery of cytological smear findings, whereas regression was defined as an improvement of cytological smear findings
2. Change in p16 (CINtec Plus test) after 3 and 6 months of follow-up

3. Overall clearance of the oncogenic HPV strains at 3 months. Clearance was defined as any hr-HPV+ (of those enumerated) at baseline that became hr-HPV- at 3 months

Overall study start date
25/09/2016

Completion date
29/01/2019

Eligibility

Key inclusion criteria
1. Female patients
2. Age 25 - 60 years
3. Histological diagnosis of CIN 1 or cytological ASC H, ASC US, LSIL associated with a positive cytological p16 or histological p16 test, or CIN 2 or HSIL
4. Signed informed consent
5. Negative pregnancy test
6. Suitable method of contraception during the treatment period for women of childbearing potential

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
222

Total final enrolment
216

Key exclusion criteria
1. Oncological or immunological disease
2. Chronic viral disease (incl. hepatitis)
3. Immunosuppressive treatment
4. Pregnancy or breastfeeding
5. Known allergy to the gel or one of its components
6. Colposcopic finding suspicious of invasive disease
7. Simultaneous participation at another clinical trial
8. For CIN 2 patients, unsatisfactory colposcopy (i.e. the transformation zone and/or the lesion is not fully visible)
9. For CIN 1 patient, risk discrepancy with cytological finding (HSIL)

Date of first enrolment
14/02/2017

Date of final enrolment
29/07/2018

Locations

Countries of recruitment
Czech Republic

Study participating centre
1 A / Centrum ambulantní gyn ekologie a primární péče, s.r.o.
Orlí 10
Brno
Czech Republic
60200

Study participating centre
1B/ GYNEKO s.r.o.
Smetanova 954
Vsetín
Czech Republic
77501

Study participating centre
2/ G CENTRUM Olomouc, s.r.o.
Horní náměstí 285/8
Olomouc
Czech Republic
77200

Study participating centre
3/ Fakultní nemocnice v Motole (University Hospital Onkogynekologická a kolposkopická ambulance
V Úvalu 84/1
Praha
Czech Republic
15000

Sponsor information

Organisation
Deflamed International s.r.o.

Sponsor details
Heřmanova 597/61
Praha
Czech Republic
17000
+43 (0)6476 805549
office@deflamed.com

Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Deflamed International s.r.o.

Results and Publications

Publication and dissemination plan
1. Publication of the results according to protocol
2. Effect of the vaginal gel on HPV, histology/colposcopy, cytology and CINtec Plus after 3 months of treatment versus watch and wait group
3. Effect of the vaginal gel on cytology and CINtec Plus after 3 months of treatment and 6 months from treatment start
4. Effect of the vaginal gel on IHC p16 positive patients in both arms
5. Effect of the vaginal gel on smear results (cytology) clustered in low- and high-risk groups
6. Effect of the vaginal gel on CIN 1 IHC p16 positive results and on CIN 2
7. Comparison of IHC p16 and CINtec Plus and HPV
8. Effects and side effects of the vaginal gel and mode of action.
9. Effect of the device on progression rates

Intention to publish date
01/01/2020

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2021	23/11/2020	Yes	No
Results article		25/05/2021	14/06/2021	Yes	No
Results article		20/06/2023	28/06/2023	Yes	No