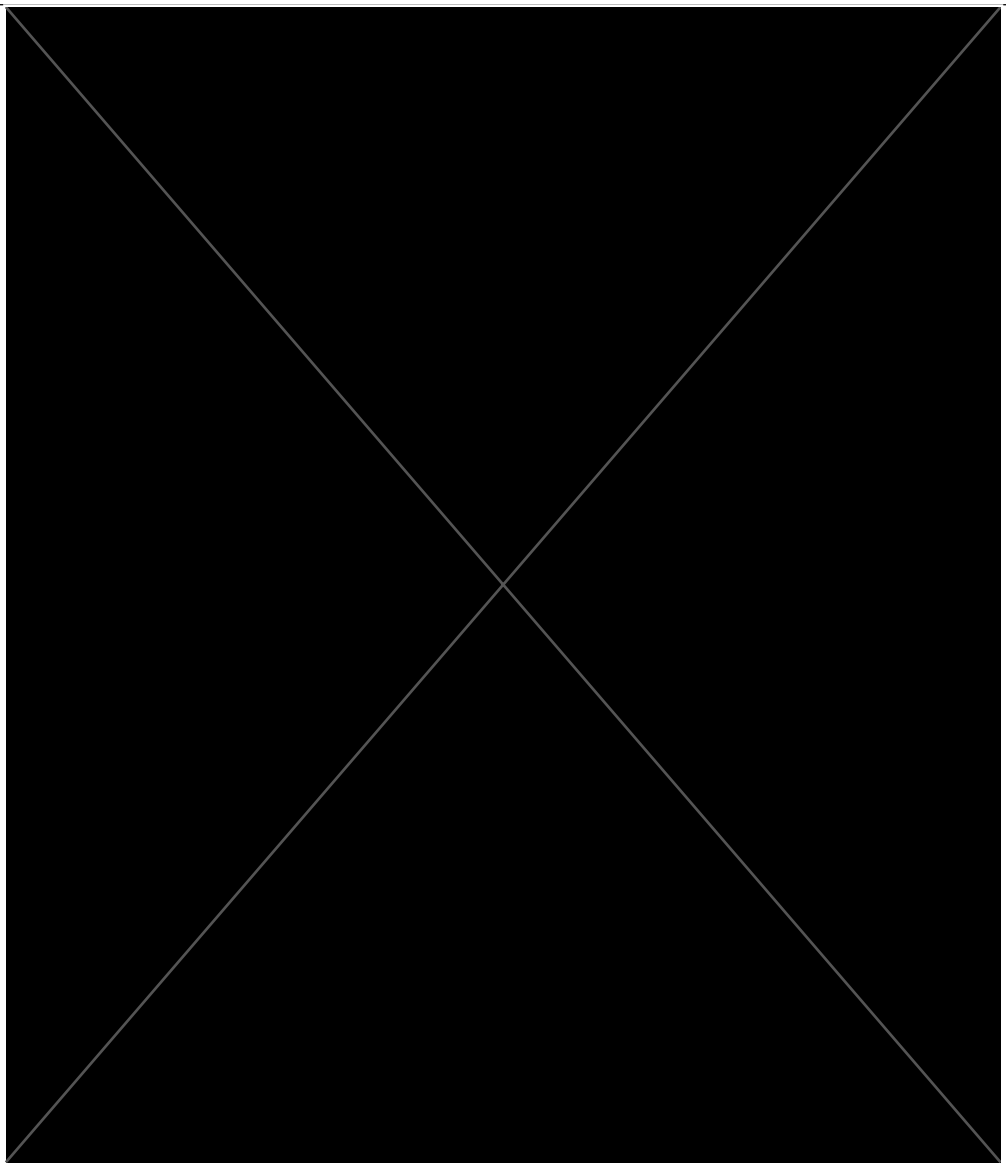
CLINICAL STUDY REPORT

1. TITEL PAGE

Drug Product:	Mifepristone (Ginestril®) tablets 50 mg
Protocol Number:	mife50
Study design	Prospective multi-center single arm open label study of efficacy, safety and acceptability of long-term weekly oral Mifepristone 50 mg as contraceptive
Study Phase:	III
Study initiation date (first patient enrolled, or any other verifiable definition)	07/08/2023
Date of early study termination.	04/07/2025
name of sponsor's responsible medical officer	Dr Rebecca Gomperts
Study Sponsor:	Stichting Women on Waves Domselaerstraat 14, 1093 MA, Amsterdam Netherlands gomperts@womenonwaves.org
	Dr Rebecca Gomperts **Phone: +31652052561** **gomperts@womenonwaves.org**
Funded by:	**CIFF and private donors**
Last Revision Date:	25 July 2025
Version Number:	1, Eudra-CT 2020-002355-38

2. SYNOPSIS

Title:	Prospective multi-center single arm open label study of efficacy, safety and acceptability of long-term weekly oral Mifepristone 50 mg as contraceptive
Clinical Phase:	III
EudraCT	2020-002355-38
Study Type:	Interventional
Investigational product:	Mifepristone tablets 50 mg (Ginestril®)
Manufacturer:	Nijpharm, Russia – pharma factory of Stada
Batches:	G03XB01, 10724
Reference product:	None
Description of Study Intervention:	All study participants will use mifepristone 50 mg once a week for 13 menstrual cycles as a contraceptive.
Study Description:	The study was a prospective multi centre open-label single-arm trial conducted in Moldova. All participants will be administered once a week mifepristone 50 mg (Ginestril®) for 13 menstrual cycles (approximately 12 months). Vaginal ultrasound were done at screening, month 3, 6, 9 and 12 or until the endometrial image is normalized. Endometrial histology was assessed voluntary at baseline and at month 12 and when a vaginal ultrasound shows endometrial thickness >15 mm or irregular cystic appearance. This was repeated until the appearance of the endometrium normalized. Urine hCG pregnancy test was done in the clinic at screening and after 3, 6, 9 and 12 months. Blood analyses (ASAT, ALAT, bilirubin, creatinine, haemoglobin, LH, FSH, oestradiol, progesterone) were performed at screening, and after 3, 6, 9 and 12 months. In case of abnormal ASAT, ALAT or bilirubin follow-up was done until normal values. ECG was done baseline, and after 6 and 12 months. Participants self-administered urine hCG pregnancy tests monthly and completed a daily side-effects and bleeding diary. At 3 and 12 months after the last mifepristone intake, participants received an on-line questionnaire about return of menstrual periods, contraceptive use, fertility, and pregnancy after the last mifepristone use.
Objectives:	**Primary Objectives:** To assess the contraceptive efficacy and safety of once a week mifepristone 50 mg. It is hypothesized that treatment with once a week mifepristone 50 mg over 12 months will yield a Pearl Index of less than 1 and does not pose any safety risks after 12 months of use. **Secondary Objectives:** To determine the side-effects and acceptability of once a week mifepristone 50 mg.
Study Population:	Number of participants planned: 949 Number of participants analysed: 181
Inclusion Criteria	● Female; ● aged 18-35; ● living in Moldova and speaking either Romanian, English or Russian; ● no desire to become pregnant within the next 12 months; ● a regular menstrual cycles with menstrual cycle length of 21-35 days; ● be willing to use mifepristone as the only contraceptive method during the study; ● expecting to have unprotected intercourse at least once a month with a partner who is not sterilized ● BMI < 35; ● be able to participate in the scheduled visits; ● be willing to fill in daily diary via app and 6-monthly questionnaires online

Description of Sites Enrolling Participants:	
Study Duration:	60 months
Duration of Treatment	13 cycles of 28 days for drug administration.
Study initiation date (first patient enrolled, or any other verifiable definition)	07/08/2023
Date of early study termination.	04/07/2025
Studied period (years):	The report covers the period of one year from august 2023 when recruitment started until august 2025.
Efficacy Results:	So far the actual use Pearl Index, which includes all pregnancies in a study and all months (or cycles) of exposure of (3/1040)*1200=3,46 as there were 3 pregnancies during all months of exposure (cycles where the participant had at least 1 time unprotected sex while participating in the study and using mifepristone 50 mg)

Safety Results:	**Liver function:** 5 (4,7%) of the 106 participants had a slightly elevated (< than 1,5 times UNL) bilirubin at one of the follow up visits. One (1,9%) of the participants had mildly elevated (< than 2 or 3 times UNL) bilirubine at the last follow up visit. 9 (8,4%) of the 106 participants developed a slightly elevated ALAT (less than 2 times ULN) 4 (3,8%) of the participants developed a slightly increased ASAT (< than 2 times UNL) and 1 (1%) an mildly elevated ASAT (2-3 times ULN) at one of the follow up visits. One participant had increased liver functions at visit 5. Bilirubine of 49 (2-3 times ULN) and ASAT 119.6, Value between 3.0-5.0 ULN: and ALAT 53.0, Value between 1.0-2.0 ULN. On July 4 2024 a new blood test was done and liver values had almost normalized, ALAT 9,8 UL, ASAT 15.93 UL and bilirubin 38,11. The participants was send for a hepatological consultation. More information will be shared in the next report. If no other causes for the increased liver functions will be found, this case might be a Hy's Law case **Endometrium:** In total 10 of the 101 10%) participants developed an endometrial thic some point during the study, of these 9 had endometrium <15 mm with the final follow up visit. Of one participant the final follow up visit still has to take place. Pathology showed that these were all cases of PAEC.
Conclusion	The study had to end preliminary because large scale fraud by Dr Irena Tripac from site 10 caused the withdrawal of donors. As a consequence not enough participants have been recruited to be able to achieve the objectives of the study to determine the Pearl Index of mifepristone as a weekly contraceptive as required by the EMA. This is still the largest study investigating the use of mifepristone 50 mg as a weekly contraceptive with 1040 exposed cycles. So far there are no concerns about safety relating to the endometrium. Cases where the endometrium thickness increased more than 15 mm were all diagnosed as PAEC and in all cased the endometrium returned to normal size without any outside intervention or shedding. One participant developed high bilirubin and ASAT at 9 months. As we are still waiting for more information about the possible relationship to the use of mifepristone, we cannot yet exclude a safety concern. Only few participants reported side effects and most women developed amenorrhea.
Date of report	01-08-2025

Summary	There is an unmet need for a contraceptive method that is easy to use, effective on demand, and free from estrogen-related side effects. Mifepristone, a well-studied progesterone receptor antagonist with a strong safety profile, was investigated for its potential as a once-weekly oral contraceptive. Mifepristone 50 mg inhibits ovulation and reduces endometrial receptivity. Prior studies showed promising contraceptive efficacy at weekly doses of 25–50 mg, with no pregnancies reported in hundreds of cycles. The current study aimed to assess long-term efficacy, safety, and acceptability of 50 mg Mifepristone taken weekly. The study was approved in Moldova in May 2022, targeting 949 women (aged 18–35) over 13 cycles. Participants used an app to log medication use, intercourse, side effects, and pregnancy tests. Safety was monitored via liver tests, ultrasounds, ECGs, and biopsies when necessary. Although recruitment began in August 2023, serious data integrity issues emerged at Site MD010 in 2025. A large-scale verification revealed widespread fraud: most participants at that site were not taking the study drug, and some were told to lie about their involvement. The site was closed, and all data from MD010 were excluded from analysis. Regulatory authorities ordered further audits and halted enrolment across all sites. Funding was withdrawn, and the study was formally closed in July 2025. Data from 173 study participants after excluding the participants from site 10 were analysed. The actual use Pearl Index so far is 3,46. The only safety concern that needs further analyses was the temporary increased liver functions above 2- 3 UNL for bilirubin and more than 3 UNL for ALAT.
Report Period	This report covers the study period from August 2023 to July 2025, excluding data from the fraudulent site.

3. TABLE OF CONTENTS

4. ABBRIVIATIONS

AE	Adverse Event
ALAT	Alanine transaminase
ASAT	Aspartate aminotransferase
CI	Confidence Interval
CL	Confirmation Letter
CIFF	Children's Investment Fund Foundation
CMP	Clinical Monitoring Plan
CONSORT	Consolidated Standards of Reporting Trials
e- CRF	(Electronic) Case Report Form
CRA	Clinical Research Associate
CRO	Contract Research Organization
DILI	Drug-Induced Liver Injury
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
ECG	Electrocardiogram
EMA	European Medicines Agency
EU	European Union
FSFI	Female Sexual Function Index
FUL	Follow Up Letter
FSH	Follicle-stimulating hormone
GBA	Glucocorticoid bioactivity
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
hCG	Human Chorionic Gonadotropin
HIPAA	Health Insurance Portability and Accountability Act
HSIL	High-grade squamous intraepithelial lesion
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
NEC	National Ethics Committee
IMV	Interim Monitoring Visit
IM	Investigator Meeting
IMP	Investigational Medicinal Product
ITF	Investigator Trial File
ISF	Investigator Site File
IU/l	International Unit(s) per Litre
ITT	Intention-To-Treat
IUD	Intrauterine Device
LH	Luteinizing hormone
LSIL	Low-grade squamous intraepithelial lesion
MMDA	Medicines and Medical Devices Agency
MVR	Monitoring Visit Report
NEC	National Ethics Committee
OC	Oral contraceptive
PAEC	PRM-associated non-physiological endometrial changes
PAP	Papanicolaou (test)
PI	Pearl Index
PM	Project Manager
PRM	Progesterone Receptor Modulator

PSV	Pre-Selection Visit
QA	Quality Assurance
SAE	Serious Adverse Event
SD	Source data
SIV	Site Initiation Visit
SmPC	Summary of Product Characteristic
SOC	System Organ Class
SOP	Standard Operating Procedure
SPR	Selective Progesterone Receptor Modulators
SUSARS	Suspected unexpected serious adverse reactions
SEA	Serious Adverse Event
TMF	Trial master File
USA	United States
US	Ultrasound
UK	United Kingdom
ULN	Upper limit of normal
VTE	Venous Tromboembolia
WHO	World Health Organisation

5. ETHICS

The study and any amendments were reviewed by an Independent Ethics Committee or Institutional Review Board.

The study and any amendments were reviewed and received approval from the Moldovan Authorities (MMDA) on 24-05-2022. Document nr. Rg02-002274

Ethical Conduct of the Study

The study at sites 1 till 9 were conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

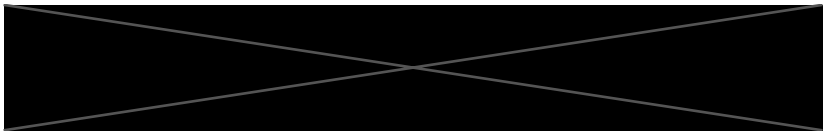
In March 2025, it was uncovered that side 10 committed severe fraud. An audit is underway and the report is expected in the beginning of September.

Patient Information and Consent

The investigator or a person designated by him/her collected written consent from each participant before her participation in the study. Prior to this, the investigator or his/her delegate informed each participant of the objectives, benefits, risks and requirements imposed by the study, as well as the nature of the IMPs.
The participant were provided with an information and consent form in clear, simple language. She had allowed ample time to inquire about details of the study and to decide whether or not to participate in the study.
Two original information and consent forms were completed, dated and signed personally by the participant and by the person responsible for collecting the informed consent.
The participant received one signed original information and consent form, the second original will be kept by the investigator.
All changes to the consent form have been NEC and MMDA-approved.

6. INVESTIGATORS AND STUDY ADMINISTRATORS

Contract Research Organization:
Bona Artis



Monitor: BonaArtis

Insurance company:
A. ASTERRA GRUP S.A.
Chisinau, Str. M. Viteazu 4 , MD-2005
IDNO: 1006600032750

Import Medication:
Gamma Logistics VR SRL

www.gammalogistics.md

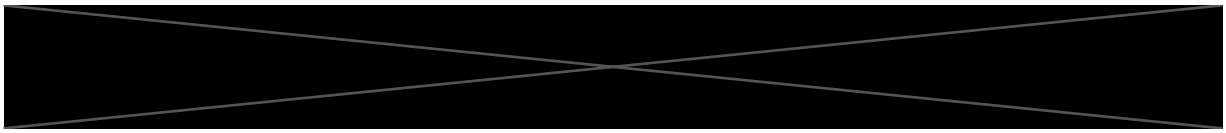
Mifepristone 50 mg Supplies:
AVERSI-PHARMA LTD
148/2 D.Agmashenebeli ave.
0 11 2 Tbilisi
GEORGIA

Central laboratory facilities:
AlfaDiagnostica laboratory.
str. N. Testemițanu, 21, Chișinău
(022) 82 44 44
info@alfalab.md

Clinical Pathology:
Oncogene (Moldova)

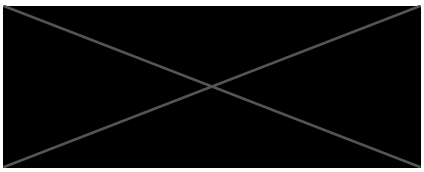
Consulting Pathologist:

Professor Alistair Williams

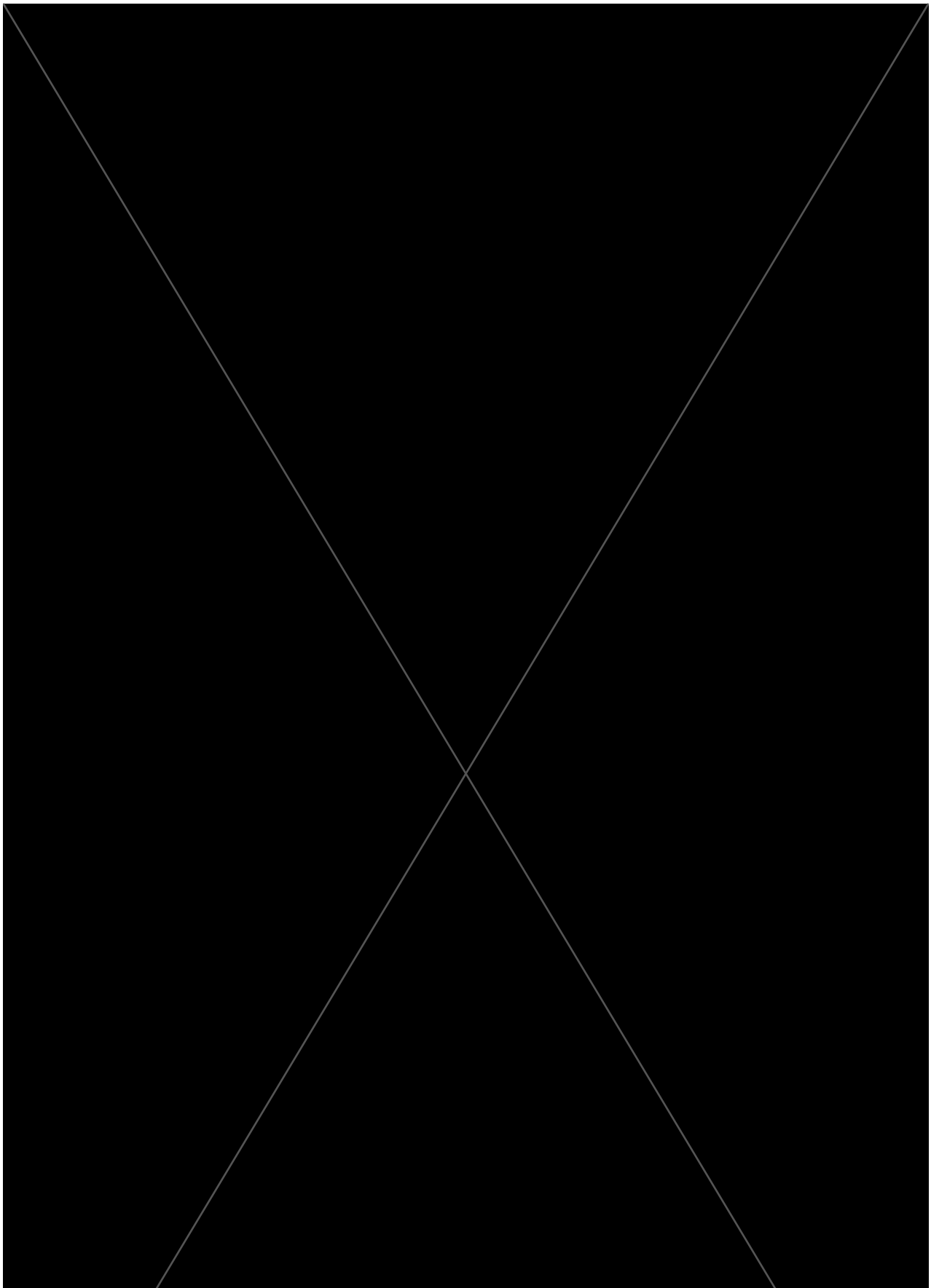


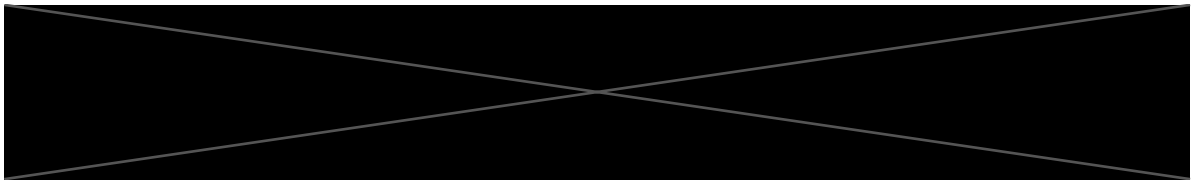
National Coordinator:
Dr. Rodica Comendant, Director at RHTC, Moldova

Study coordinator:
Dr Rebecca Gomperts, Director Stichting Women on Waves (Study Sponsor)
Domselaerstraat 14, Amsterdam
Netherlands
Email: *gomperts@womenonwaves.org*



Local Investigators





7. INTRODUCTION

Background and Rationale

There is a growing need for new contraceptive methods that align with the preferences and lifestyles of modern women. An ideal contraceptive should be easy to use correctly, free from systemic side effects and health risks, effective on demand, and independent of partner involvement.

Mifepristone, a progesterone receptor antagonist developed in the late 1980s, has been widely studied and approved for use in medical abortion in combination with prostaglandin analogues such as misoprostol. Beyond its role in abortion, Mifepristone is approved in the United States for the long-term treatment of Cushing's syndrome under the brand name Korlym, at daily doses of up to 1200 mg. Its extensive clinical use and well-established safety profile make it a promising candidate for contraceptive development.

Prior research has shown that daily doses of 0.5 mg and weekly doses of 2.5–5 mg induce significant endometrial changes without fully inhibiting ovulation. A weekly dose of 10 mg reduced fertility but was associated with an unacceptably high failure rate. In a dose-finding study, weekly doses of 25 mg and 50 mg showed promising efficacy. No pregnancies were reported across 234 and 222 cycles, respectively, in users of these doses.

The 50 mg weekly dose was associated with higher rates of amenorrhea and reduced menstrual bleeding, likely indicating stronger suppression of ovulation and endometrial activity. This dose was selected for the current long-term study due to its favorable efficacy and safety profile.

8. INVESTIGATIVE MEDICAL PRODUCT

The investigational drug, mifepristone 50 mg (Ginestril®), is a light-yellow round tablet with diameter 8 mm and height 3 mm. The drug is delivered by the pharmacy in blisters of 30, accompanied by a patient information leaflet, contained within carton boxes. Ginestril® is manufactured by Obninsk, Russia.
The holder of the registration certificate in Moldova was SA „Nijfarm", Rusia 603950, Nijnii Novgorod GSP-459, str. Salganskaya, 7 Tel.: (831) 278-80-88 Fax: (831) 430-72-28.

Study product will be packaged and labelled according to Good Manufacturing Practices in Georgia, where the product is registered and on the market. The study medication will be imported from Georgia where it is available and packaged in 3 blisters of 10 tablets, in total 30 tablets per package. Package insert is available in Russian and Romanian.

Storage

The IMP was stored with a temperature log at each side at room temperature [i].

Chemical structure

Chemically, Mifepristone is identified as 11β-(4-(dimethylamino)phenyl)-17α-(1-propynyl)estra-4,9-dien-17β-ol-3-one. It is an estrane steroid derivative of norethindrone and functions as a selective progesterone receptor modulator (SPRM). Mifepristone binds with high affinity to progesterone and glucocorticoid

receptors, and to a lesser extent to androgen receptors. Its ATC classification is G03XB01: sex hormones and modulators of the genital system – specifically, progesterone receptor modulators.
Unlike estrogen-containing contraceptives, Mifepristone is not associated with common estrogen-related adverse effects such as weight gain, libido reduction, depression, headache, or increased risk of venous thromboembolism, making it a potentially more acceptable contraceptive option.

Mechanism of Action in Contraception

At low doses, Mifepristone exerts contraceptive effects via two primary mechanisms:

1. Inhibition of Ovulation: When administered during the follicular phase—just before the luteinizing hormone (LH) surge—Mifepristone delays the LH peak, extends the follicular phase, and thus postpones ovulation without affecting the luteal phase.
2. Endometrial Alteration: It reduces endometrial receptivity, preventing successful implantation of the blastocyst.

Treatment administered

Women will receive 1 tablet of mifepristone 50 mg per week for 13 cycles (12 months = one year). If a woman forgets the weekly mifepristone 50 mg (Gynestril®), she should administer the last missed tablet as soon as she remembers and take the next tablets at the usual times. If she takes the pills 2 days or more delayed, she should use an additional contraceptive method (barrier method) for the next 7 days and perform an extra pregnancy test 3 weeks later.

Due to the unavailability of sufficient Stada 50 mg tablets in Moldova (the local authorization expired in 2023), the study drug was imported from Georgia, where it remained approved.

9. STUDY OBJECTIVES

The primary objective was to evaluate the long-term efficacy, safety, and acceptability of Mifepristone 50 mg administered once weekly as a contraceptive.

OBJECTIVES	**ENDPOINTS**	**JUSTIFICATION FOR ENDPOINTS**
Primary		
To assess the contraceptive efficacy and safety of once-a week mifepristone 50 mg.	Occurrence of pregnancy during treatment caused by method failure.	The occurrence of pregnancy in the treatment period caused by treatment failure will be used to measure the efficacy of the treatment
	Proportion of women with endometrium thickness >15 mm, endometrium with irregular cystic appearance on US at baseline, and after 3, 6, 9, and 12 months.	The ultrasonic image of the endometrium and histology will be used to establish the safety of the treatment
	Proportion of women with ALAT, ASAT elevation three times above normal or bilirubin two times above normal after 3, 6, 9, and 12 months	Laboratory values will establish impact on liver function and the safety of the treatment

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
	Proportion of women with adverse event / serious adverse event.	AE/SAE will establish the safety of the treatment
Secondary		
To determine the side-effects and acceptability of once a week mifepristone 50 mg	Evaluation of serum levels of LH, FSH, oestradiol, progesterone	Many hormonal contraceptives have negative side effects such as depression, loss of libido, weight gain, increased irregular bleeding patterns, that decrease the acceptability of the contraceptive method. Absence of these side effects will increase acceptability and compliance and thus increase efficacy
	Proportion of women with amenorrhea	
	Proportion of women with endometrial changes (PAEC) confirmed by biopsy at baseline, after 12 months and time to normalisation.	
	Occurrence of pregnancy during treatment caused by user failure.	
	Mean value of quality of life questionnaire (EQ-5D-5L) at baseline, and after 6 and 12 months.	
	Proportion of women who use antidepressants at enrolment and during the study.	
	Proportion of women with dysmenorrhea (diary continued measurement) during the study.	
	Proportion of women with acne occurrence (diary continued reporting) during the study.	
	Proportion of women with side-effects (headache, nausea, breast pain, dry eyes) (diary continued reporting) during the study.	
	Mean weight changes at 3, 6, 9, 12 months compared to baseline.	
	Proportion of women with vaginal bleeding (diary continued measurement).	
	Libido: mean value of Female Sexual Function Index (FSFI) at baseline, and after 6 and 12 months.	

10. REGULATORY APPROVAL

The study received approval from the Moldovan Medicines and Medical Devices Agency (MMDA) on 24 May 2022. Notably, 50 mg Mifepristone had previously been registered in Moldova for daily use until March 2023.

11. STUDY DESIGN

The study is a prospective single arm open label study in Moldova to determine the Pearl Index and monitor safety and acceptability of weekly 50 mg mifepristone for 12 months in Moldova.

There is no stratification.

To assess contraceptive efficacy with statistical robustness (assuming a Pearl Index target), a total of 12,337 cycles were required. To meet this threshold, 949 women aged 18–35 were planned to be enrolled and followed for one year (13 cycles).

Efficacy was monitored daily diary using a mobile app

- Frequency of intercourse

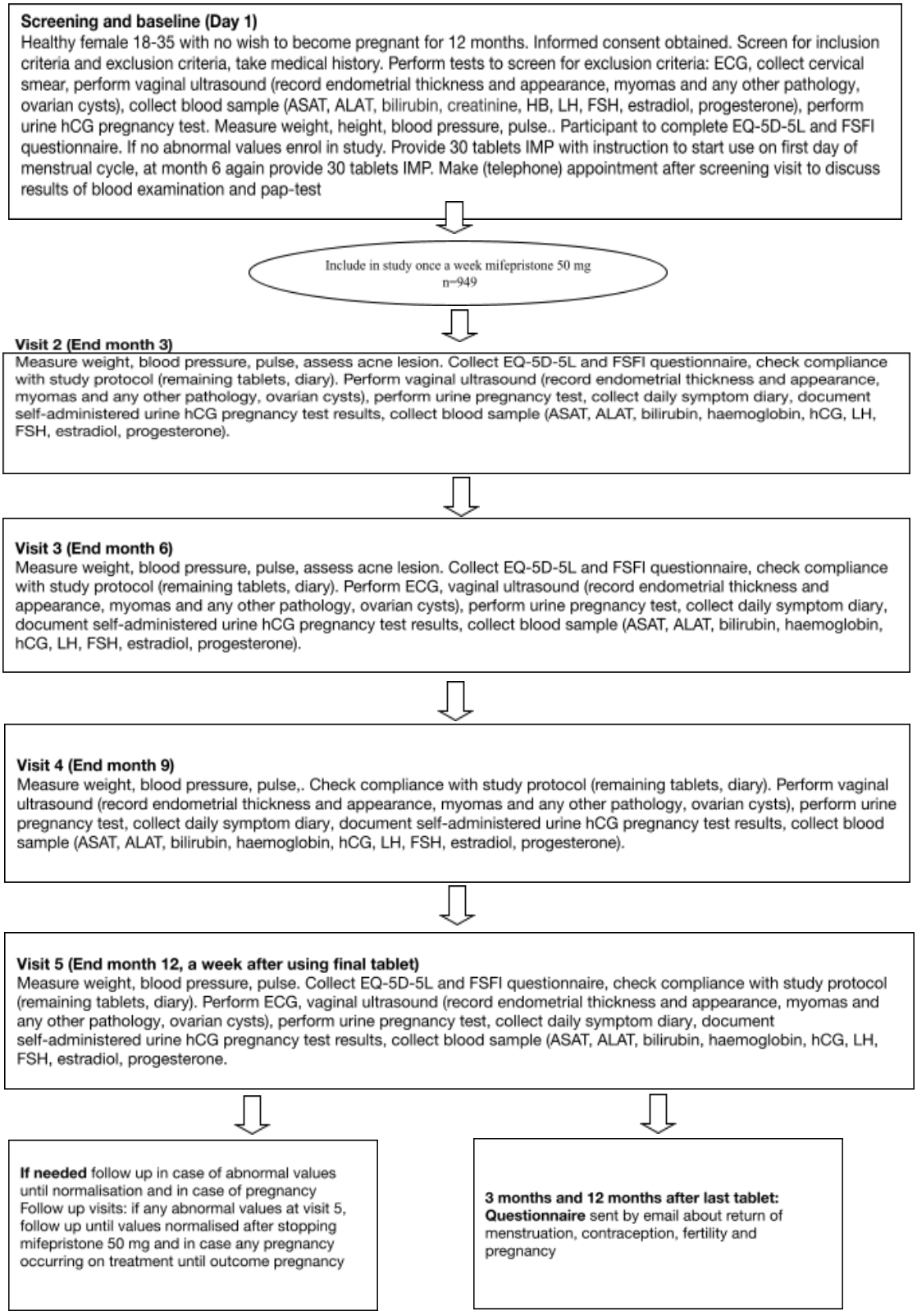
- Medication use
- Pregnancy testing results of monthly and 3 monthly pregnancy tests

Safety was monitored by:

- Vaginal ultrasound done at screening, and after 3, 6, 9, 12 months or until normalised appearance.
- Blood tests (liver functions [ASAT, ALAT, bilirubin] creatinine and haemoglobin) at screening, months 3, 6, 9, 12 months or until liver function tests values normalised.
- Endometrial histology, assessed if vaginal ultrasound shows irregularities or is > 15 mm until the appearance of the endometrium is normal.
- ECG at enrolment, 6 months and 12 months.

Acceptability was measured by:

- Weight,
- EQ-5D-5L will be taken at baseline, months 6 and 12
- FSFI will be taken at baseline, months 6 and 12
- Daily dairy for registering side effects and bleeding
- Any adverse events or complaints


Screening and baseline (Day 1)
Healthy female 18-35 with no wish to become pregnant for 12 months. Informed consent obtained. Screen for inclusion criteria and exclusion criteria, take medical history. Perform tests to screen for exclusion criteria: ECG, collect cervical smear, perform vaginal ultrasound (record endometrial thickness and appearance, myomas and any other pathology, ovarian cysts), collect blood sample (ASAT, ALAT, bilirubin, creatinine, HB, LH, FSH, estradiol, progesterone), perform urine hCG pregnancy test. Measure weight, height, blood pressure, pulse.. Participant to complete EQ-5D-5L and FSFI questionnaire. If no abnormal values enrol in study. Provide 30 tablets IMP with instruction to start use on first day of menstrual cycle, at month 6 again provide 30 tablets IMP. Make (telephone) appointment after screening visit to discuss results of blood examination and pap-test
Include in study once a week mifepristone 50 mg
n=949
Visit 2 (End month 3)
Measure weight, blood pressure, pulse, assess acne lesion. Collect EQ-5D-5L and FSFI questionnaire, check compliance with study protocol (remaining tablets, diary). Perform vaginal ultrasound (record endometrial thickness and appearance, myomas and any other pathology, ovarian cysts), perform urine pregnancy test, collect daily symptom diary, document self-administered urine hCG pregnancy test results, collect blood sample (ASAT, ALAT, bilirubin, haemoglobin, hCG, LH, FSH, estradiol, progesterone).
Visit 3 (End month 6)
Measure weight, blood pressure, pulse, assess acne lesion. Collect EQ-5D-5L and FSFI questionnaire, check compliance with study protocol (remaining tablets, diary). Perform ECG, vaginal ultrasound (record endometrial thickness and appearance, myomas and any other pathology, ovarian cysts), perform urine pregnancy test, collect daily symptom diary, document self-administered urine hCG pregnancy test results, collect blood sample (ASAT, ALAT, bilirubin, haemoglobin, hCG, LH, FSH, estradiol, progesterone).
Visit 4 (End month 9)
Measure weight, blood pressure, pulse,. Check compliance with study protocol (remaining tablets, diary). Perform vaginal ultrasound (record endometrial thickness and appearance, myomas and any other pathology, ovarian cysts), perform urine pregnancy test, collect daily symptom diary, document self-administered urine hCG pregnancy test results, collect blood sample (ASAT, ALAT, bilirubin, haemoglobin, hCG, LH, FSH, estradiol, progesterone).
Visit 5 (End month 12, a week after using final tablet)
Measure weight, blood pressure, pulse. Collect EQ-5D-5L and FSFI questionnaire, check compliance with study protocol (remaining tablets, diary). Perform ECG, vaginal ultrasound (record endometrial thickness and appearance, myomas and any other pathology, ovarian cysts), perform urine pregnancy test, collect daily symptom diary, document self-administered urine hCG pregnancy test results, collect blood sample (ASAT, ALAT, bilirubin, haemoglobin, hCG, LH, FSH, estradiol, progesterone.
If needed follow up in case of abnormal values until normalisation and in case of pregnancy
Follow up visits: if any abnormal values at visit 5, follow up until values normalised after stopping mifepristone 50 mg and in case any pregnancy occurring on treatment until outcome pregnancy
3 months and 12 months after last tablet:
Questionnaire sent by email about return of menstruation, contraception, fertility and pregnancy

Period of Study / Visit #	Screening	Treatment /Baseline	Treatment					
Visit #	**1**		**2**	**3**	**4**	**5**		
Time	**Day 1**		**End Month 3**	**End Month 6**	**End Month 9**	**End Month 12**	**Month15**	**Month 24**
Procedure								
Informed consent	X							
Inclusion/exclusion criteria review	X							
Medical history	X							
Cervical smear	X							
Urine hCG pregnancy test on-site	X		X	X	X	X		
Concomitant medication review, including assessment of antidepressant usage	X		X	X	X	X		
Height	X							
Weight	X		X	X	X	X		
Vital signs (blood pressure, pulse)	X		X	X	X	X		
EQ-5D-5L questionnaire	X			X		X		
FSFI questionnaire	X			X		X		
Vaginal ultrasound	X		X	X	X	X		
ECG	x			x		x		
Blood sample (ASAT, ALAT, bilirubin, haemoglobin, creatinine)	X		X	X	X	X		
Voluntary endometrial biopsy	X					X		
Blood sample (LH, FSH, oestradiol, progesterone)	X		X	X	X	X		
Discuss results of cervical smear, blood tests		X						
Deliver study product		X		X				
Self-administered urine hCG pregnancy test results collected at follow-up visit			X	X	X	X		
Daily symptom diary collected			X	X	X	X		
Adverse event review and assessment, including assessment of side effects			X	X	X	X		
Compliance control			X	X	X	X		
On-line questionnaire about return of menstruation, contraception, fertility and pregnancy							X	X

12. INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Female, Age 18-35,
2. Living in Moldova and speaking and understanding either English, Moldavian or Russian.
3. No desire to become pregnant within the next 12 months, be willing to use mifepristone as the only method of contraception for 12 months
4. A menstrual cycle of 21-35 days, unless current hormonal contraceptives
5. After depot-provera (3 month injectable) at least 3 cycles of 21-35 days
6. BMI < 35
7. Be willing to use mifepristone as the only contraceptive method during the study
8. expecting to have unprotected intercourse at least once a month with a partner who is not sterilized
9. Ability to take oral medication and be willing to adhere to the contraceptive regimen
10. Be able to participate in the scheduled visits
11. Be willing to fill in daily diary and 6-monthly questionnaires via app
12. Be willing to provide signed and dated informed consent form about participation in the study

If women fulfil the inclusion criteria, they will be screened for exclusion criteria. Screening procedures are:

- pregnancy test
- ultrasound (endometrium)
- blood analyses (ALAT, ASAT, bilirubin, creatinine and haemoglobin)
- cervical smear

13. EXCLUSION CRITERIA

An individual who meets any of the following criteria has been excluded from participation in this study:

1. Not fitting into inclusion criteria
2. Current pregnancy
3. Lactation
4. Undiagnosed abnormal vaginal bleeding
5. Signs of current endometritis, incomplete abortion after miscarriage or induced abortion, retained placental rests after delivery or pelvic inflammatory disease (PID)
6. Abnormal PAP smear at screening which requires colposcopy and/or biopsy according to the Moldova national guideline for abnormal pap-test
7. Known subfertility or history of ectopic pregnancy
8. Any previous or current malignancy including breast cancer
9. Family history of endometrial cancer
10. Known BRCA gene mutation
11. Previous or current liver illness or infection or ASAT, ALAT or bilirubin > 2 ULN at screening
12. Intracavitary abnormalities on vaginal ultrasound at screening, including intracavitary polyps or myomas, irregular cystic endometrium, endometrium > 15 mm, or an obvious aspect of hydrosalpinx
13. Gastric bypass
14. Known allergy to mifepristone
15. Using high doses of corticosteroids or any drugs that may interact with mifepristone - these include hydantoins (e.g. phenytoin), barbiturates (e.g. phenobarbital), primidone, carbamazepine, rifampicin, oxcarbazepine, topiramate, rifabutin, felbamate, ritonavir, nelfinavir, griseofulvin and products containing St. John's wort (Hypericum perforatum)
16. Treatment with another investigational drug (until next normal period after stopping any other trial);
17. Undiagnosed reason for severe anaemia or increased creatinine
18. Severe hypertension (180 mm Hg or more systolic, or/and 110 mm Hg or more diastolic) (hypertension with medical treatment allowed)
19. Unable to comply with the trial protocol

14. DATA QUALITY ASSURANCE

Quality control (QC) procedures have been implemented beginning with the data entry system and data QC checks that run on the database were generated. Any missing data or data anomalies were communicated to the site(s) for clarification/resolution.
Following written Standard Operating Procedures (SOPs), the monitors verified that the clinical trial is conducted and data are generated and biological specimens are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

Investigators meetings
The Investigator Meeting was performed on 14Oct2022 and an other training meeting took place in 11November 2023, in Chisinau, Republic of Moldova. All training materials are included in Investigator Site File.
Before initiating any activities with the sites the involved CRA received a study specific training on all essential documents of this Clinical Trial. The training is documented and filed in the TMF.
The study specific training focussed on the following documents:

- Protocol
- Monitoring Plan
- Master versions of used ICFs
- IB
- eCRF Manual
- eDiary Manual
- Safety Management Plan
- SAE, Pregnancy forms
- Investigator Manual
- SmPC of Mifepristone 50mg

The training on new/updated documents and study procedures was provided to required team members by means of team meetings (online and/or face to face) or self-training requests.

On site training:
Each study team at the approved study sites was trained by CRA during the SIV and the training was registered in the training form, part of ISF. The following documents were covered as part of SIV presentation:

- Study protocol and flow chart
- IMP handling and accountability
- Study supplies
- ISF maintenance
- GCP and ALCOA+ compliance
- eCRF completion
- eDiary
- Safety reporting

Additional training, on updated documents, Amendments, were provided by CRA for Investigators during IMV. The training was registered in the training log, part of ISF, and reported in IMV report and FUL.

Ongoing training
The CRA assigned to the site was responsible to ensure the appropriate training on all relevant documentation and processes for all new site staff.

Source Data Verification
The main goal of SDV is to ensure that the study data were collected in appropriate way, corresponds to ALCOA+ principles:

- The screened/enrolled subjects are real and exists;

- Each screened subject has a SD file, containing information about medical history and participation, concomitant disease, medication and participation in the trial;
- The relevant subject information has been accurately transferred to eCRF;
- ICFs are completely and correctly signed;
- Inclusion/exclusion criteria are satisfied for the enrolled subjects;
- Laboratory samples were sampled according to the protocol, laboratory reports were assessed by Investigator and available in subject file;
- All data transferred into eCRF was 100% verified against SD.

On site responsibilities
Each clinical site will perform internal quality management of study conduct, data and biological specimen collection, documentation and completion. An individualized quality management plan is being developed to describe a site's quality management.
The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

Protocol deviations:

A protocol deviation is any noncompliance with the clinical trial protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), or Standard Operating Procedures (SOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.
It is the responsibility of the investigator to use continuous vigilance to identify and report deviations within 15 working days of identification of the protocol deviation, or within 15 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents and reported to Women on Waves. Protocol deviations must be sent to the reviewing NEC and MDDA as per their policies. The investigator is responsible for knowing and adhering to the reviewing requirements. Further details about the handling of protocol deviations will be included in the SOP.

Each protocol deviation detected by CRA, Investigator was registered in the PD log, part of ISF. CRA also reported PDs in the Monitoring Visit reports. Based on reported PD the Sponsor excluded subject's data from data analysis. Examples of PDs:

- Initiated screening before obtaining the subject Inform Consent;
- Not respected eligibility criteria for enrolled subjects;
- Not performed safety laboratory procedures, omitted tests;
- Use of prohibited medication;
- Used of IMP that was affected by temperature excursion;
- Visits are not performed according to protocol timelines;

All PDs have been reviewed by PM and the Sponsor was informed accordingly. The critical PDs, that can affect the safety of subjects, have been reported within 24h to BonaArtis PM.

15. CLINICAL MONITORING

After the complete Clinical Trial approval and study sites supplies/IMP delivery the SIVs were performed. The visits will be documented in the SIV report. The first IMV took place within 2 weeks after the enrolment (randomization) of first subject in the Clinical Trial at the respective Study Site. In total at least 7 IMVs per study site are planned within this Clinical Trial. The frequency was adapted to the site activity and speed of enrolment, identified issues during previous IMV, etc.
Each Monitoring Visit Report was prepared according to the corresponding SOP of BonaArtis. The CRA prepared the draft of the report and FUL within 5 working days and sent the report to PM for review. The report must be reviewed by PM within 5 working days and all comments/remarks clarified with responsible CRA. The draft of the report will be submitted to the Sponsor responsible PM for final approval. The CRA will sent the final FUL to the site, to be filed also in ISF. Each approved report will be hand signed by CRA and PM. The copy of the SIV report will be placed also in ISF. All Monitoring Reports will be filed in TMF.

16. PARTICIPANT CONFIDENTIALITY, DATA COLLECTION AND STORAGE

Confidentiality

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible. The CRF only contains and is stored with anonymised data so that no participant can be identified. SD (paper and/or electronic) will be stored at the research centers in the ITF.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, are exported to the sponsor. These data will not include the participant's contact details or identifying information. Individual participants and their research data can only be identified by a unique study identification number (formed by combination study centre and participant number). The study data entry and study management systems used by clinical sites and by the research staff is secured and password protected. Original data will be saved in Castor at Leiden Medical University.

The study monitor, other authorized representatives of the sponsor, representatives of the NEC, regulatory agencies and MMDA may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site permits access to such records.

Data collection and storage

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing, Institutional policies, or sponsor requirements.

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the study visit worksheets have been provided for use as source document worksheets for recording data for each participant enrolled in the study. Data recorded in Castor derived from source documents should be consistent with the data recorded on the source documents.

Clinical data (including AEs), concomitant medications, expected adverse reactions data and clinical laboratory data will be entered into Castor, a 21 CFR Part 11-compliant data capture system. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate.

Clinical data will be entered directly from the source documents in the eCRF by the PI in the clinics or by a dedicated person to be hired for this purpose.

Data collected for this study will be analysed and stored at the Leiden Medical University using Castor. After the study is completed, the de-identified, archived data will be transmitted to and stored at the Castor, for use by other researchers including those outside of the study. Permission to transmit data to the Castor will be included in the informed consent.

Study documents should be retained for a minimum of 2 years after the last approval of a marketing application in an International Conference on Harmonisation (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the study intervention. No records will be destroyed without the written consent of the sponsor, if applicable. All SD and CT documentation will be archived electronically at least for 25 years at the study sites.

All source data (subject file, medical records, signed ICF, etc.) and ITF (Investigator Trial File) will be stored in the research site/Hospital archive for 25 years (according to Moldovan legislation)
All eCRF data, TMF will also be stored for 25 years

Storage biological specimens

Pap-smears will be stored according to Moldavian regulations. Histology slides will be assessed by two pathologists. Storage will be according to Moldavian regulations. Photos of the de-identified histology slides will be stored in the eCRF for 25 years

Blood samples are stored at the local laboratory or according to their internal SOP and Quality Standards and after that are destroyed.

During the conduct of the study, an individual participant can choose to withdraw consent to have biological specimens stored for future research. However, withdrawal of consent with regards to biosample storage may not be possible after the study is completed.
When the study is completed, access to study data and/or samples will be provided through the study sponsor Women on Waves

Publication and Data Sharing Policy

This study will be conducted in accordance with the following publication and data sharing policies and regulations of Public Access Policy, which ensures that the public has access to the published results of public funded research.
Every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers after the completion of the primary endpoint by contacting the Primary Investigator Kristina Gemzell Danielsson.

17. FINANCING AND INSURANCE

This study was financed by the Sponsor.
The subjects will not be compensated for participation in this study but will receive reimbursements for travel and other expenses.
During the study, the subjects were insured as the study subjects according to the local laws.
If health damage occurred due to administration of the study product or medical procedure per study Protocol, the subjects received free qualified medical care to the extent paid by Insurance Company.
For participants who became pregnant during the study and wanted to terminate the pregnancy, the Sponsor compensated for a surgical or medical abortion. There were no participant who wanted to continue the pregnancy.

18. SITE UPDATES AND INSPECTION OUTCOMES

- **May and June, 2023,** Initiation visits of sites 1 to 9
- **August 4, 2023, First Participant First Visit**
- **May 31, 2024:** A new site (MD010) was added.

- **June 7, 2024:** Sites 3, 4, and 8 were closed due to lack of enrolment.
- **October 2024:** MMDA inspections of sites MD001, MD006, and MD009 revealed no major or critical findings.
- **October 1, 2024:** Recruitment at MD010 was temporarily paused due to backlog; resumed on November 11, 2024, after resolution.
- **March 14, 2025:** Due to shipment delays, all sites received a temporary stop on new recruitment.

19. SERIOUS MISCONDUCT AT SITE MD010

In April 2025, concerns emerged regarding potential data falsification at site MD010. With NEC approval, the study team initiated direct subject verification via phone from May 5–7, 2025. Among 364 enrolled subjects:

- The majority reported **not taking the investigational product**.
- Several described using hormonal contraceptives (e.g., 21 active pills + 1 week off).
- Two reported having IUDs.
- One subject was pregnant, despite no reported pregnancy by site investigators.
- Some participants disclosed they had been **coached to lie** about their participation.

On **May 6, 2025**, the Sponsor:

- Notified regulatory authorities (MMDA and NEC) of suspected fraud.
- Issued a formal halt of the study at site MD010.

Subsequent events included:

- **May 11, 2025:** The Sponsor informed the site PI of the study termination and initiated withdrawal and safety follow-up plans.
- **May 13, 2025:** MMDA conducted an unannounced inspection; the PI fled the site, and remaining staff denied involvement.
- **May 14, 2025:** MMDA issued an official order halting the study at MD010.
- **May 15, 2025:** MMDA conducted an inspection at BonaArtis.
- **June 2, 2025:** MMDA mandated a temporary enrolment suspension across all sites, pending Sponsor and internal audits.

Due to the severity of fraud at MD010, study funders suspended their support, leading to **study closure in July 2025**.

20. STUDY CLOSE-OUT AND FINAL NOTES

The COV will be performed according to SOP-005-CT_Close-out Monitoring. The CRA main activities during COV will consist in:

- To perform the inventory of IMP (drug accountability log, dispense log, return logs, destruction confirmation), storage conditions (temperature logs);
- Study supplies and remained unused documents are returned to the CRO or destroyed at the site and a destruction confirmation is filed into ISF;
- All ISF logs are verified, closed and scans collected for TMF;
- All queries are resolved, the eCRF pages are signed by PI;
- The Investigators are informed about records retention and archiving responsibilities, potential audits and inspections and obligation to inform accordingly the CRO/Sponsor, results publication policy;

For sites that were prematurely closed, CRA ensured that Sponsor/CRO Notification about activities termination is filed in the ISF.

- Safety follow-up and close-out visits were completed at site MD006.
- Remaining site visits are scheduled for the end of **July 2025**.

21. SCOPE OF THIS REPORT

This report summarizes the study outcomes over a **two-year period** (August 2023 to July 2025), excluding all data from site MD010 due to confirmed misconduct and data falsification.

22. STUDY RESULTS

We excluded all 470 participants recruited by side 10 because of the fraud, 178 participants remain of whom 58 participants completed the study.

Including participants of side 10

Study status	total
completed study	58
early stop mife	26
ineligible	11
mife started	137
Not Set	408
not started	3
pregnancy	3
withdrawn IC	1
Grand Total	**647**

Excluding participants of side 10

Count of Participant	
Side 1-9	
completed study	58
early stop mife	26
ineligible	9
mife started	60
Not Set	18
not started	3
pregnancy	3
withdrawn IC	1
Grand Total	**178**

Ineligible

After completing recruitment, 9 Participants were Ineligible to participate in the study.

	ineligible	reason
MD_001.008	1	the subject refused because of cervical pathology
MD_001.011	1	refused to continue the study
MD_001.014	1	refused to perform endometrial biopsy
MD_001.022	1	refused endometrial biopsy and PAP test to perform
MD_001.031	1	abnormal PAP test
MD_001.034	1	went abroad (see info query first date mife did not take)
MD_001.072	1	the patient had ASC-US on cervical cytology and refused
MD_006.003	1	menorrhagia, posthemorrhagic anemia of moderate severity, occured before MIFE 50 participation unwilling to participate
MD_009.004	1	Screening failure
Grand Total	**9**	

Discontinuation

In total 26 participants who discontinued. Of these 21 were enrolled by site 9 and was caused by the relocation of the PI to another clinic than enrolled the participants and the clinic where she continued to work was far away for most participants.

Reasons for discontinuation were:

	early stop mife	reason
MD_001.021	1	lost to follow up after 6 months
MD_005.004	1	The patient changed her life abroad due to family reasons after 3 cycles
MD_006.008	1	The study was stopped due to sponsor decision after 5 cycles
MD_006.010	1	The study was stopped due to sponsor decision after 1 cycle
MD_007.001	1	lost to folllow up after 4 cycles
MD_009.002	1	The patient moved her life in another country
MD_009.003	1	The patient changed her plans. She no longer wants contraception due to personal reasons after 6 months
MD_009.006	1	The patient is no longer comfortable attending site visits and has no available free time. As a result, she has decided to withdraw from the study. After 7 cycles
MD_009.011	1	The patient relocated and is no longer able to access the study site after 9 cycles
MD_009.012	1	The patient no longer requires contraception due to changes in personal circumstances after 1 cycle
MD_009.015	1	The patient expressed lack of motivation to continue participation in the study after 7 cycles
MD_009.016	1	The patient decided to switch to a different contraceptive method outside of the study protocol after 3 cycles
MD_009.017	1	The patient was lost to follow-up despite repeated contact attempts after 7 cycles
MD_009.019	1	The patient was lost to follow-up despite repeated contact attempts after 2 cycles
MD_009.021	1	The patient had difficulty adhering to study requirements and chose to withdraw voluntarily after 2 cycles
MD_009.023	1	The patient no longer requires contraception due to changes in personal circumstances after 7 cycles
MD_009.026	1	The patient moved or relocated and could not continue study visits at the current site after 1 cycle
MD_009.028	1	the subject did not complete the dairy,for this reason it is not known for sure when she stopped taking the medicine
MD_009.029	1	The patient felt that the method did not align with her personal or cultural beliefs and decided to discontinue after 5 cycles
MD_009.030	1	The patient is planning to become pregnant and therefore discontinued participation after 4 cycles
MD_009.033	1	The patient no longer requires contraception due to changes in personal circumstances after 3 cycles
MD_009.034	1	The patient felt that the method did not align with her personal or cultural beliefs and decided to discontinue after 0 cycles
MD_009.035	1	The patient is planning to become pregnant and therefore discontinued participation after 4 cycles
MD_009.036	1	The patient is no longer comfortable attending site visits and has no available free time. As a result, she has decided to withdraw from the study after 5 cycles
MD_009.037	1	The patient is no longer comfortable attending site visits and has no available free time. As a result, she has decided to withdraw from the study after 1 cycle
MD_009.038	1	The patient is experiencing family conflicts with her partnership and can no longer attend study visits after 6 cycles
total	**26**	

23. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

All 178 recruited participants were women age 18 till 35. Mean age: 26

Mean height = 1.67 m (1.52- 1.83 m)
Mean weight =64 kg (40-94 kilo)
Mean BMI = 23 (range 16- 33)

number of children	0	1	2	3	0	Grand Total
Count of participants	5	35	25	6	107	178

education level	**less than high school**	**high school**	**university**	**postgraduate**	**total**
Total	7	21	136	14	178

	completed study	early stop mife	ineligible	mife started	Not Set	not started	pregnancy	withdrawn IC	
MD_001,001	1								
MD_001,002	1								
MD_001,003	1								
MD_001,004	1								
MD_001,005	1								
MD_001,006	1								
MD_001,007	1								
MD_001,008			1						
MD_001,009	1								
MD_001,010	1								
MD_001,011			1						
MD_001,012	1								
MD_001,013								1	
MD_001,014			1						
MD_001,015	1								
MD_001,016	1								
MD_001,017	1								
MD_001,018	1								
MD_001,019	1								
MD_001,020	1								
MD_001,021		1							
MD_001,022			1						
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MD_001,027	1								
MD_001,028	1								
MD_001,029	1								
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MD_001,031			1						
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MD_001,098						1			
MD_001,100						1			
MD_002,001						1			
MD_005,001	1								
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MD_006,009								1	
MD_006,010		1							
MD_006,011							1		
MD_007,001		1							
MD_007,003						1			
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MD_009,062						1			
MD_009,063						1			
MD_009,064						1			
MD_009,065					1				
Grand Total	**58**	**26**	**9**	**60**	**18**	**3**	**3**	**1**	**178**

Row Labels	AGE	HEIGHT (in M)	WEIGHT in kg	BMI
MD_001.001	28	1,65	76	28
MD_001.002	25	1,73	60	20
MD_001.003	32	1,64	74	28
MD_001.004	35	1,67	86	31
MD_001.005	34	1,67	53	19
MD_001.006	22	1,7	88	30
MD_001.007	32	1,58	70	28
MD_001.008	31	1,74	80	26
MD_001.009	34	1,68	56	20
MD_001.010	27	1,75	63	21
MD_001.011	35	1,69	74	26
MD_001.012	35	1,65	60	22
MD_001.013	30	1,56	55	23
MD_001.014	34	1,64	74	28
MD_001.015	26	1,7	70	24
MD_001.016	24	1,7	84	29
MD_001.017	28	1,6	66	26
MD_001.018	33	1,78	81	26
MD_001.019	32	1,63	68	26
MD_001.020	29	1,66	60	22
MD_001.021	33	1,6	58	23
MD_001.022	35	1,58	45	18
MD_001.023	33	1,67	68	24
MD_001.024	31	1,65	65	24
MD_001.025	23	1,52	61	26
MD_001.026	23	1,69	65	23
MD_001.027	27	1,7	60	21
MD_001.028	24	1,55	48	20
MD_001.029	23	1,7	61	21
MD_001.030	24	1,63	86	32
MD_001.031	30	1,64	57	21
MD_001.032	33	1,67	62	22
MD_001.033	19	1,58	52	21
MD_001.034	19	1,72	75	25
MD_001.035	33	1,65	60	22
MD_001.037	18	1,6	55	21
MD_001.038	21	1,6	85	33
MD_001.039	24	1,65	60	22
MD_001.040	34	1,75	85	28
MD_001.041	23	1,68	75	27
MD_001.042	25	1,62	61	23
MD_001.043	28	1,63	64	24
MD_001.044	28	1,62	52	20
MD_001.045	30	1,6	54	21
MD_001.046	25	1,71	65	22
MD_001.047	21	1,63	44	17
MD_001.048	22	1,6	53	21
MD_001.049	26	1,64	52	19
MD_001.050	27	1,68	62	22
MD_001.051	27	1,68	60	21
MD_001.052	31	1,74	70	23
MD_001.053	18	1,7	64	22
MD_001.054	22	1,79	68	21
MD_001.055	22	1,65	53	19
MD_001.056	34	1,63	80	30
MD_001.057	18	1,65	65	24
MD_001.058	23	1,6	60	23
MD_001.059	20	1,75	67	22
MD_001.060	19	1,53	44	19
MD_001.061	34	1,72	65	22
MD_001.062	19	1,68	59	24
MD_001.063	24	1,76	61	20
MD_001.064	23	1,65	55	20
MD_001.065	24	1,63	70	26
MD_001.066	24	1,68	70	25
MD_001.067	28	1,54	62	26
MD_001.068	21	1,65	52	19
MD_001.069	32	1,57	59	24
MD_001.070	23	1,76	60	19
MD_001.071	24	1,64	62	23
MD_001.072	32	1,6	80	31
MD_001.073	26	1,56	49	20
MD_001.074	20	1,68	74	26
MD_001.075	21	1,8	61	19
MD_001.076	31	1,7	64	22
MD_001.077	28	1,65	64	24
MD_001.078	26	1,58	52	21
MD_001.080	35	1,72	73	25
MD_001.081	24	1,73	61	20
MD_001.082	28	1,64	54	20
MD_001.083	35	1,65	75	28
MD_001.084	24	1,6	48	19
MD_001.085	24	1,68	57	20
MD_001.086	27	1,7	65	22
MD_001.087	30	1,68	55	19
MD_001.088	29	1,6	46	18
MD_001.089	27	1,6	50	20
MD_001.090	20	1,56	76	31
MD_001.092	26	1,56	54	22
MD_001.093	27	1,68	58	21
MD_001.094	25	1,6	40	16
MD_001.095	27	1,7	62	21
MD_001.096	24	1,64	89	33
MD_001.098	24	1,72	80	27
MD_001.100	24	1,67	70	25
MD_002.001	29	1,68	67	24
MD_005.001	26	1,72	94	32
MD_005.002	29	1,7	64	22
MD_005.003	35	1,65	73	27
MD_005.004	30	1,57	74	30
MD_006.002	28	1,72	85	29
MD_006.003	31	1,65	72	26
MD_006.004	35	1,65	71	26
MD_006.005	29	1,6	84	33
MD_006.006	32	1,65	72	26
MD_006.007	27	1,64	50	19
MD_006.008	27	1,65	65	24
MD_006.009	31	1,63	54	20
MD_006.010	29	1,61	69	27
MD_006.011	30	1,56	48	20
MD_007.001	18	1,63	45	17
MD_007.003	32	1,65		
MD_008.001	19	1,53	43	18
MD_009.001	28	1,7	64	22
MD_009.002	20	1,67	56	20
MD_009.003	25	1,7	59	20
MD_009.004	30	1,7	56	19
MD_009.005	29	1,64	62	23
MD_009.006	28	1,7	87	30
MD_009.007	29	1,67	63	23
MD_009.008	34	1,76	65	21
MD_009.009	27	1,6	51	20
MD_009.010	22	1,73	63	21
MD_009.011	20	1,6	56	22
MD_009.012	29	1,73	62	21
MD_009.013	33	1,62	68	26
MD_009.014	32	1,64	64	24
MD_009.015	28	1,6	70	27
MD_009.016	34	1,7	52	18
MD_009.017	26	1,73	59	20
MD_009.018	28	1,68	63	22
MD_009.019	30	1,62	61	23
MD_009.020	32	1,77	61	19
MD_009.021	28	1,72	60	20
MD_009.022	22	1,76	70	23
MD_009.023	21	1,68	55	19
MD_009.024	28	1,75	63	21
MD_009.025	32	1,68	65	23
MD_009.026	22	1,63	45	17
MD_009.027	19	1,83	65	19
MD_009.028	22	1,65	65	24
MD_009.029	33	1,7	62	21
MD_009.030	27	1,64	50	19
MD_009.031	27	1,64	54	20
MD_009.032	21	1,65	54	20
MD_009.033	23	1,65	70	26
MD_009.034	18	1,68	74	26
MD_009.035	30	1,68	71	25
MD_009.036	31	1,74	81	27
MD_009.037	23	1,72	46	16
MD_009.038	30	1,7	65	22
MD_009.039	20	1,7	62	21
MD_009.040	27	1,7	52	18
MD_009.041	22	1,73	82	27
MD_009.042	22	1,72	75	25
MD_009.043	22	1,68	67	24
MD_009.044	22	1,72	67	23
MD_009.045	22	1,7	72	25
MD_009.046	28	1,7	67	23
MD_009.047	19	1,73	68	23
MD_009.048	21	1,7	72	25
MD_009.049	25	1,7	67	23
MD_009.050	23	1,76	74	24
MD_009.051	30	1,71	62	21
MD_009.052	27	1,68	62	22
MD_009.053	23	1,74	69	23
MD_009.054	24	1,79	64	20
MD_009.055	30	1,67	64	23
MD_009.056	20	1,73	87	29
MD_009.057	29	1,63	58	22
MD_009.058	19	1,68	70	25
MD_009.059	24	1,76	88	28
MD_009.060	21	1,77	60	19
MD_009.061	24	1,73	75	25
MD_009.062		1,7	51	18
MD_009.063	23	1,65	85	31
MD_009.064		1,79	56	17
MD_009.065		1,74	70	23
Mean	**25,7**	**1,61**	**62**	**22**

24. EFFICACY STUDY RESULTS

The EMA scientific committee advises that a Pearl-Index (PI) for method failure of less than 1 with a difference between the upper and lower confidence interval of less than 1, should be used in this study and not a typical use PI which is caused by method and patient failure. If we assume the true PI is 1, 12337 cycles are needed.[2] To meet this requirement, we had planned to enrol 949 participants for 1 year (or 13 menstrual cycles)[3] Unfortunately the study had to be halted because of fraud committed by side 10 and the withdrawal of funding as a result.

Women kept an electronic daily diary during the trial where they note when the medicines have been taken, bleeding, monthly pregnancy tests performed and any effects and secondary outcomes.
A tablet count check at each visit and if women forgot pills the remaining tablets will be returned to the clinic and compared with the diaries.

The study provided all participants 12 commercially available hCG urine pregnancy tests. Participants self-administered a pregnancy test once a month at home and marked the result in the diary. Participants were instructed to call the investigator in case of a positive self-administered pregnancy test.

Urine hCG pregnancy tests were performed by the investigator at the study site at screening, at the 3, 6, 9 and 12 months visit.

A positive urine hCG pregnancy test (whether conducted at home or in the clinic) was confirmed by serum hCG test and, if positive, an ultrasound examination was performed for confirmation and dating.

If the participant in the study had a confirmed pregnancy, she was withdrawn from the study.

Pregnancy rates will be described by Pearl Index including all pregnancies during treatment.

Unprotected cycles

There were in total 1040 unprotected cycles from the 146 participants who filled in the diary (data from the participants of side 10 are excluded). An unprotected cycle means that a women had sex without using any other form of contraceptive at least once per months.

Pregnancies

In total 3 pregnancies were reported during the study. All pregnancies were also reported as SAE.

- 1 participant MD_005.002 became pregnant before she started with the mifepristone tablets as she did not start mifepristone at LMP but later. She had an abortion.
- 1 pregnancy of participant MD_001.067 was ectopic. This was also reported as a SAE. There is not enough information is available to determine if she used the mifepristone tablets properly as she completed the diary after the pregnancy was detected. She had an emergency operation.
- 1 pregnancy happened after the participant MD_006.009 forgot to use the mifepristone tablet as indicated in her diary. She had an abortion.

This information gives an actual use Pearl Index, which includes all pregnancies in a study and all months (or cycles) of exposure of (3/1040)*1200=3,46 as there were 3 pregnancy during all months of exposure (cycles where the participant had at least 1 time unprotected sex while participating in the study and using mifepristone 50 mg)

Pregnancy 1

studyNumber	reportedDate	mife use	seks	pregtest	bleeding
abortion	02/02/2024				
LMP	03/03/2024				
expected LMP start Mife	03/04/2024				
MD_005.002	15/04/2024	1	1	no	0
MD_005.002	22/04/2024	1	0	yes, negative	0
MD_005.002	29/04/2024	1	0	no	
MD_005.002	06/05/2024	1	0	yes, negative	0
MD_005.002	13/05/2024	0	0	yes, positive	0

Pregnancy 2

	reportedDate	mife use	seks	pregtest	bleeding
MD_006.009	13/01/2025	0	0	no	1
MD_006.009	21/02/2025	1	0	no	0
MD_006.009	22/02/2025	0	1	no	0
MD_006.009	23/02/2025	0	0	no	0
MD_006.009	24/02/2025	0	0	no	0
MD_006.009	25/02/2025	0	0	no	0
MD_006.009	26/02/2025	0	1	no	0
MD_006.009	27/02/2025	0	0	no	0
MD_006.009	28/02/2025	1	0	no	0
MD_006.009	01/03/2025	0	1	no	0
MD_006.009	02/03/2025	0	0	no	1
MD_006.009	03/03/2025	0	0	no	1
MD_006.009	04/03/2025	0	0	no	1
MD_006.009	05/03/2025	0	0	no	0
MD_006.009	06/03/2025	0	0	no	0
MD_006.009	07/03/2025	1	1	no	1
MD_006.009	08/03/2025	0	0	no	1
MD_006.009	09/03/2025	0	0	no	1
MD_006.009	10/03/2025	0	0	no	1
MD_006.009	11/03/2025	0	0	no	1
MD_006.009	12/03/2025	0	1	no	0
MD_006.009	13/03/2025	0	0	no	1
MD_006.009	14/03/2025	0	0	no	1
MD_006.009	15/03/2025	0	1	no	0
MD_006.009	16/03/2025	0	0	no	1
MD_006.009	17/03/2025	0	0	no	0
MD_006.009	18/03/2025	0	0	no	0
MD_006.009	19/03/2025	0	1	no	0
MD_006.009	20/03/2025	0	1	no	0
MD_006.009	21/03/2025	1	1	no	0
MD_006.009	22/03/2025	0	1	no	0
MD_006.009	23/03/2025	0	0	no	0
MD_006.009	24/03/2025	0	1	no	0
MD_006.009	25/03/2025	0	0	no	0
MD_006.009	26/03/2025	0	1	no	0
MD_006.009	27/03/2025	0	0	no	0
MD_006.009	28/03/2025	1	1	no	0
MD_006.009	29/03/2025	0	1	no	1
MD_006.009	30/03/2025	0	0	no	0
MD_006.009	31/03/2025	0	0	no	1
MD_006.009	01/04/2025	0	1	no	1
MD_006.009	02/04/2025	0	1	no	0
MD_006.009	03/04/2025	0	1	no	0
MD_006.009	04/04/2025	1	0	no	0
MD_006.009	05/04/2025	0	0	no	0
MD_006.009	06/04/2025	0	0	no	1
MD_006.009	07/04/2025	0	0	no	1
MD_006.009	08/04/2025	0	0	no	1
MD_006.009	09/04/2025	0	0	no	1
MD_006.009	10/04/2025	0	0	no	0
MD_006.009	11/04/2025	1	0	no	0
MD_006.009	12/04/2025	0	1	no	0
MD_006.009	13/04/2025	0	0	no	0
MD_006.009	14/04/2025	0	1	no	0
MD_006.009	15/04/2025	0	0	no	0
MD_006.009	16/04/2025	0	1	no	0
MD_006.009	17/04/2025	0	1	no	0
MD_006.009	18/04/2025	1	0	no	0
MD_006.009	19/04/2025	0	1	no	0
MD_006.009	20/04/2025	0	1	no	0
MD_006.009	21/04/2025	0	0	no	0
MD_006.009	22/04/2025	0	0	no	0
MD_006.009	23/04/2025	0	1	no	0
MD_006.009	24/04/2025	0	0	no	0
MD_006.009	25/04/2025	1	0	no	0
MD_006.009	26/04/2025	0	0	no	0
MD_006.009	27/04/2025	0	0	no	0
MD_006.009	28/04/2025	0	0	no	0
MD_006.009	29/04/2025	0	0	no	0
MD_006.009	30/04/2025	0	1	no	0
MD_006.009	01/05/2025	0	1	no	0
MD_006.009	02/05/2025	1	0	no	0
MD_006.009	03/05/2025	0	1	no	0
MD_006.009	04/05/2025	0	1	no	0
MD_006.009	05/05/2025	0	0	no	0
MD_006.009	06/05/2025	0	1	no	0
MD_006.009	07/05/2025	0	1	yes, positive	0
MD_006.009	08/05/2025	0	1	yes, positive	0
MD_006.009	09/05/2025	1	1	yes, positive	0

Pregnancies after end of study

After the end of the study, 1 pregnancy was reported after the final visit and mifepristone was not used anymore. She decided to have an abortion.

	pregtest +	date first mife	Last visit 5	date conception	
MD-06.002	03/Jan/25	07/Dec/23	03/12/2024	15/12/2024	was already at end of study and stopped using mife after 3-12 but starting again with remaining tablets after 2 weeks on 19/Dec/24

Unprotected cycles	2023					2024												2025										total unprote
participant	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul			
MD_001.001		1	0	1	1	1	1	1	0	1	1	0	0	0	0												7
MD_001.002		1	1	1	1	1	1	1	1	1	1	1	1	1	1												13
MD_001.003		0	0	1	1	1	1	0	1	1	1	1	1	1	1	1											11
MD_001.004			0		0	1	1	1	1	1	1	1	1	1	0	0											8
MD_001.005		0	1	0	0	0	0	0	0	0	0	1	1	1	1												5
MD_001.006			0	0	0	1	1	1	1	1	1	1	1	1	1	1											10
MD_001.007		1	1	1	1	1	1	1	1	1	1	1	1	1	1												13
MD_001.009			0	1	1	1	1	1	1	1	1	1	1	1	0	1	1										12
MD_001.010			1	1	1	1	1	1	1	1	1	1	1	1	1	1											13
MD_001.012				1	1	1	1	1	1	1	1	1	1	1	1	1	1										13
MD_001.013		0	0	0	0	0	0	0	0																		0
MD_001.015				1	1	1	1	1	1	1	1	1	1	1	1	1											12
MD_001.016	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1											14
MD_001.017			1	1	1	1	1	1	1	1	1	1	1	1	1												12
MD_001.018						1	1	1	1	1	1	1	1	1	1												9
MD_001.019			1	1	1	1	1	1	1	1	1	1	1	1	1												13
MD_001.020			0	1	1	1	1	1	1	1	1	1	1	1	1	1											13
MD_001.021			1	0	0	1	1	0	0																		3
MD_001.023			1	1	1	1	1	0	1	1	1	1	1														9
MD_001.024			1	0	0	1	1	1	1	1	1	1	1	1	1	1											11
MD_001.025			0	1	1	1	1	1	0	1	1	0	1	1	1												10
MD_001.026			1	0	1	0	1	1	1	1	1	1	1	1	1	1	0										11
MD_001.027				0	1	1	1	1	1	1	1	1	1	1	1	1											12
MD_001.028			0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1							16
MD_001.029				1	0	0	0	0	0	1	1	0	1	1	1	1											8
MD_001.030					0	0	0	0	0	0	1	1	1	1	1	1											8
MD_001.032						0	0	1	0	1	0	0	1	1	1	1	1	1	1								8
MD_001.033								1				1	1	1	1	1	1	1	1	1							9
MD_001.035								1	1	1	1	1	1	1	1	1	1	1	1	1							13
MD_001.037								1	1	0	1	1	1	1	1	1	1	1	1	1	1						13
MD_001.038								1	0	0	1	1	1	1	1	1	1	1	1	0							10
MD_001.039								0	0	0	0	0	0	0	0	1	1	1	1								4
MD_001.040									1	1	1	1	1	1	1	1	1	1	1	1	1						13
MD_001.041								1	1	1	1	1	1	1	1				1	1							11
MD_001.042									1	1	1	1	1	1	1	1	1	1	1	1	1						14
MD_001.043										0	0	1	1	0	1	0	0	0	0	0	1	0	0	0			4
MD_001.044										1	1	1	1	1	1												6
MD_001.045										1	0	0	0	1	0	0	0	0	0	0	0						2
MD_001.046									0	1	1	1	1	1	1						1						7
MD_001.047												1	1	1	0	1	1	1	1	1	1						10
MD_001.048													1	1	1	1	1										5
MD_001.049													1	1	1	1	1	1	1	1	1	1	1				12
MD_001.050												1	1	1	1	1	1	1	1	0	1	1	1	1			12
MD_001.051																1	1	1	1	1	1	1					8
MD_001.052															1	0	0	0	0	0	1	1	1				4
MD_001.053													1	0	1	1	1	1	1	1	1	1					9
MD_001.054															1	0	0	0	1	1	1	0	0				4
MD_001.055															1	1	1	1	1	1	1	1					9
MD_001.056															1	1	1	1	1	1	1						8
MD_001.057																1	1	1	1	1	1	1	1				9
MD_001.058			1	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1			19
MD_001.059															1	1	1	1	1	1	1	1					8
MD_001.060															1	1	1	1	1	1	1	1	1				10
MD_001.061																1	1	1	1	1	1	0	0	1			8
MD_001.062																	0	0	1	1	0	0					2
MD_001.063																	0	0	1	0							1
MD_001.064																	1	1	1	1	1	1	1	1			8
MD_001.065																0	0	0	0	0	1	1					2
MD_001.066																	1	0	1	1		1					4
MD_001.067																	1	1	1	1							4
MD_001.068																	1	1	1	0							3
MD_001.069																						1					1
MD_001.073																					0	1	1	0			2
MD_001.074																			0	0	0	0	0	0			0
MD_001.075																			0	1	1	1	1	1			5
MD_001.076																			0	0	0	0	0	0			0
MD_001.077																			0	1	1	1	0	0			3
MD_001.078																			1								1
MD_001.080																		1	1	1	1	1	1	1			7
MD_001.081																			1	1	1	1	1	1			6
MD_001.082																			1	0		1	1	1			4
MD_001.083																			1	1	1	1	1	1			6
MD_001.084																					0	0	0				0
MD_001.085																					0	1					1
MD_001.086																								0			0
MD_001.087																							1	1			2
MD_001.089																								0			0
MD_001.090																					0	0	1	0			1
MD_001.092																						1					1
MD_001.093																					1	1	1	1			4
MD_005.001								1	1	1	1	1	1	1	1	1	1	1	1	1							13
MD_005.002										1	0																1
MD_005.003												1	1	1	1	1	1	1	1	1	1	1	1	1			13
MD_005.004												0	1	1	1	1	1										4
Md_006.002							1	1	1	1	1	1	1	1	1	1	1										13
MD_006.004							1	1	1	1	1		1	1	1	1	1										12
MD_006.005							1	1	1	1	1	1	1	1	1	1	1										13
MD_006.006										0	1	1	1	1	1	1	1	1	1	1	1	1					12
MD_006.008																			0	0		1	1	0			2
MD_006.009																			1	1	1	1	1				5
MD_006.010																							1	1			2
MD_007.001				1	1	1	1	1	1	1																	6
MD_007.003															0	1	1	1	1	1	1	1	1				8
MD_009.001				1	1	1	1	1	1	1	1	1	1	1	1												12
MD_009.002				1	1	1	1	1	1	1	1	1	1	1													11
MD_009.003				0	1	1	1	1	1	1	1	1	1	1													10
md_009.005					1	1	1	1	1	1	1	1	1	1	1	1	1										13
MD_009.006					1	1	1	1	1	1																	6
MD_009.007				0	0	1	1	1	1	1	1	1	1	1	1	1	0										11
MD_009.008					0	1	1	1	1	1	1	1	1	1	1	1	0										11
MD_009.009					0	1	1	1	1	1	1	1	1	1	1	1	1										12
MD_009.010					0	1	1	1	1	1	1	1	1	1	1	1	1										12
MD_009.011						0	1	1	1	1	1	1	1	1													8
MD_009.012							1	0	0					0													1
MD_009.013						0	1	1	1	1	1	1	1	1	1	1	1	1									12
MD_009.014						0	1	1	1	1	1	1	1	1	1	1	1										12
MD_009.015						1	0	1	1	1	1	1	1														7
MD_009.016						0	1	1	1																		3
MD_009.017							1	1	1	1	1	1	1														7
MD_009.018							1	1	1	1	1	1	1	1	1	1	1										12
MD_009.019							1	1	1																		3
MD_009.020							1	1	1	1	1	1	1	1	1	1	1										12
MD_009.021								1	1	1																	3
MD_009.022							0	1	1																		2
MD_009.023								0	1	1	0																2
MD_009.024								1	1	1	1	1	1	1	1	1	1	1	1	1							13
MD_009.025									1																		1
MD_009.026									1	1																	2
MD_009.027									1						0												1
MD_009.029									1	1	1	1	1														5
MD_009.030									1	1	1	1	1														5
MD_009.031									1	1	1	1	1	1	1	1	1	1	1	1	1						13
MD_009.032										1	1	1	1	1	1	1	1	1	1	1	0						11
MD_009.033									0	1	1	1															3
MD_009.035										1	1	1															3
MD_009.036											1	1	1	1	1												5
MD_009.037											1	1															2
MD_009.038											1	1	1	1	1	1											7
MD_009.039											1	1															2
MD_009.040												0	1	1	1	1	1	1	1	1	1	1	1				11
MD_009.041															1	1	1	1	1	1	1						7
MD_009.042															1	1	1	1	1	1	1						8
MD_009.044															0	1											1
MD_009.045															1	1											2
MD_009.046															0	1											1
MD_009.047																1											1
MD_009.048															1	1	1	1	1	1	1	1					8
MD_009.049																1	1	1	1	1	1						6
MD_009.050												1	1	1	1	1	1	1	1	1	1	1					11
MD_009.051																1	1	1	1	1	1	1					7
MD_009.052																1	1	1	1	1	1						6
MD_009.053																1	1	1	1	1							5
MD_009.054															0	1	1	1	1	1	1	1					7
MD_009.056																	0	1	1	1	1						4
MD_009.057																	1	1	1	1	1						5
MD_009.058																	0	1	1	1	1						4
MD_009.059																		0	1	1	1	1	0				4
GrandTotal	1	4	14	22	31	43	53	59	60	63	68	68	65	69	73	61	54	55	51	41	41	27	16	2			1040

25. HORMONES

Progesterone levels:

When the measured P level was >2 µg/l, ovulation likely occurred. When the P level was approximately 5 µg/l, the patients were highly likely to be between days 2 and 3 postovulation.[4]

The progesterone tests in the study participants showed:

- At baseline 54 Of 178 (30%) had a progesterone lever higher than 2 µg/l, indicating that ovulation likely occurred.
- At months 3, 39 of the 106 (37%) had a progesterone lever higher than 2 µg/l, indicating that ovulation likely occurred.
- At months 6, 17 of 81 (21%) had a progesterone lever higher than 2 µg/l, indicating that ovulation likely occurred.
- At months 9, 13 of 64 (20%) had a progesterone lever higher than 2 µg/l, indicating that ovulation likely occurred.
- At months 12, 22 of 61 (36%) had a progesterone lever higher than 2 µg/l, indicating that ovulation likely occurred.
- Of all 174 participants whose progesterone was measured at baseline, 70 (40%) had at least once a progesterone lever higher than 2 µg/l , during the follow up visits indicating that ovulation likely occurred at least once at some point during the study.

Estradiol levels

After menopause, estradiol levels typically fall below 10-30 pg/mL. None of the participants had an estradiol level less than 27.

Estradiol levels					
N	**164**	**102**	**78**	**62**	**61**
Visit	**1**	**2**	**3**	**4**	**5**
Average	144	123	126	142	120

FSH levels

FSH					
N	172	106	81	64	62
Visit number	1	2	3	4	5
Average	5,85	5,50	5,60	5,43	5,08

LH Levels

LH					
N	172	106	81	64	62
Visit nr	1	2	3	4	5
Average	11,8	9,1	8,8	9,3	9,3

LH	Column Labels				
Row Labels	**1**	**2**	**3**	**4**	**5**
MD_001,001	5,4	8,6	3,9	47	3
MD_001,002	4,8	17,9	1,7	11,3	8,9
MD_001,003	4,4	4,9	9,4	4,3	7,2
MD_001,004	16,1	9	8,5	7,9	12,9
MD_001,005	8,8	9,8	18,2	10,1	5,7
MD_001,006	7,7	6,3	5,7	5,5	5,4
MD_001,007	4,8	12	12,4	9,3	12,4
MD_001,008	8,4				
MD_001,009	4,7	12,1	16,8	12,7	21,1
MD_001,010	12	13,7	16,4	10,3	1,7
MD_001,011	10,7				
MD_001,012	12,6	5,9	10,2	14,8	4,2
MD_001,013	3,9	21	5,8		
MD_001,014	4,1				
MD_001,015	10	13,4	18,6	2,7	36,4
MD_001,016	13,6	8,7	5,6	9,7	6,8
MD_001,017	8,3	7,8	10,3	17,1	7,2
MD_001,018	3,7	5,7	11,1	9	5,3
MD_001,019	6,1	5,7	5,6	5,6	3,7
MD_001,020	35,9	6,8	10,7	6	1,9
MD_001,021	39,2	11,6			
MD_001,022	10				
MD_001,023	14,8	3,1	7,2	8,4	8,6
MD_001,024	18	4,7	2,8	7	7,9
MD_001,025	2,7	15,3	10	11,4	12,3
MD_001,026	5,8	7,1	4,9	2,8	8,6
MD_001,027	10,1	11,4	6,4	19,6	5,6
MD_001,028	38,4	7,7	5,2	3,5	4
MD_001,029	7,7	5,7	6,6	6,7	18,7
MD_001,030	5,8	14	23,1	4,4	28,2
MD_001,031	20,2				
MD_001,032	3,2	4,2	4,8	4,28	3,9
MD_001,033	2,3		10,8	36,4	7,6
MD_001,034	9				
MD_001,035	12	7,7	3,5	18,7	10,1
MD_001,037	14,8	11,5	9,5	5,7	4,4
MD_001,038	7,8	6,6	5,7	8	6,2
MD_001,039	10,2	8,1	8,9	2,5	47,5
MD_001,040	3	3,1	3,5	11,8	5
MD_001,041	3,4	11,9	6	4,2	3,8
MD_001,042	18,2	18,1	14,2	9,77	6
MD_001,043	9,6		18,9	5,2	4,7
MD_001,044	6	11,3	10,9	4,8	2,8
MD_001,045	5,1	8,1	2,3		
MD_001,046	6,8	6,3	6	3,5	5,3
MD_001,047	11,8	10,8	6,4	6,1	
MD_001,048	4,9	3,4	8,8	6,1	
MD_001,049	4,2	11,6	7		
MD_001,050	5,5	4,5		17,4	9,4
MD_001,051	6,2	8,1	3,8		
MD_001,052	16,8	10,8	8,1		
MD_001,053	6,1	4,1	1,8	5	
MD_001,054	4,8	11,8	8,5		
MD_001,055	1,7		11		
MD_001,056	8,2	12,5	8,4	8,4	
MD_001,057	11,4		6		
MD_001,058	8,4		3,9		
MD_001,059	19,8	3,4	15,3	8,6	
MD_001,060	5,8	12,5	4	3,2	
MD_001,061	5	11,5	8,1		
MD_001,062	6,2	7,4	6,5		
MD_001,063	8,6	7,4			
MD_001,064	23,3	7,6	5,1		
MD_001,065	1,7	3,9	10,3		
MD_001,066	16,2	12,3	19,6		
MD_001,067	16,3				
MD_001,068	12,6		11		
MD_001,069	3,3				
MD_001,070	11				
MD_001,071	5,3				
MD_001,072	8,4				
MD_001,073	1,6				
MD_001,074	5,6	11,7			
MD_001,075	6,2	6,5			
MD_001,076	6,4	8,6			
MD_001,077	5,4	3,6			
MD_001,078	6,19				
MD_001,080	4,8	6,7			
MD_001,081	9,1	14,8			
MD_001,082	38,2	5,6			
MD_001,083	5,2	6,2			
MD_001,084	11,2	11,5			
MD_001,085	5,3	3,7			
MD_001,086	8				
MD_001,087	7,3				
MD_001,088	8,6				
MD_001,089	15,4				
MD_001,090	3,2	6,8			
MD_001,092	6,3				
MD_001,093	5,6	5,9			
MD_001,094	10,7				
MD_001,095	4,4				
MD_001,096	8,1				
MD_001,098	56,1				
MD_001,100	50,2				
MD_002,001	18				
MD_005,001	10	7,5			
MD_005,002					
MD_005,003					
MD_005,004	12,4				
MD_006,002	16	6,3	9	3,3	19,3
MD_006,003	7,7				
MD_006,004	6,5	6,4	7,4	2,9	2,6
MD_006,005	2,1	6,7	2,1	2,5	2,4
MD_006,006	10,6	13,5	8,9	5,6	6,3
MD_006,007	19,1				
MD_006,008	5,7	36,6			6,5
MD_006,009	12,7	4,6			
MD_006,010	8,27				13,7
MD_006,011	14,2				
MD_007,001	11,2	10,4			
MD_007,003	2,6				
MD_008,001					
MD_009,001	56,9	7,4		29,1	4,7
MD_009,002	11,4	12,7		6,9	
MD_009,003	51,3		7,5		
MD_009,004	29,9				
MD_009,005	4,9	10,6		11,4	11,7
MD_009,006	16,9		23,7		
MD_009,007	14,1	9,9		27	10,3
MD_009,008	7,6	11,2		13	6,9
MD_009,009	6,8	12,4		8,7	7,8
MD_009,010	9	5,5		6,8	11,2
MD_009,011	6,6	4,9			
MD_009,012	30,8		5,3		
MD_009,013	5,9	8,1		10	5,2
MD_009,014	7,7	10,8			5,3
MD_009,015	37,6			4,6	
MD_009,016	3	1,7			
MD_009,017	23,6	17,2			
MD_009,018	18,5	10,4		15,3	4,6
MD_009,019	28,5				
MD_009,020	8,7	8,7			9,2
MD_009,021	12,1				
MD_009,022	4,5		6,7	5,1	6,6
MD_009,023	3,4		4,8		
MD_009,024			19		9,3
MD_009,025	5			10,9	7,5
MD_009,026	24,7				
MD_009,027	8,4	10	9,5		31,4
MD_009,028	7,4				
MD_009,029	2,21		3,3		
MD_009,030	6,9	5,8			
MD_009,031	10,9	7,2		3,3	
MD_009,032	31,8	13,7		11,8	6,3
MD_009,033	6,4	9,7			
MD_009,034	27,1				
MD_009,035	11,6	17,1			
MD_009,036	9	7,3			
MD_009,037	11,9				
MD_009,038	50,8		12,5		
MD_009,039	6,6	7,9		15,1	
MD_009,040	9,9	5,5		6,6	
MD_009,041	7,8	13,5	9		
MD_009,042	8,2		26,7		
MD_009,043	3,4				
MD_009,044	7				
MD_009,045	9,6	9,7	4,5		
MD_009,046	29,2	8,7	8,6		
MD_009,047	22,4		1,5		
MD_009,048	8,6		18,7		
MD_009,049	5,5	2,8			6,6
MD_009,050	5,6		9,5		
MD_009,051	7,5	5	4,8		
MD_009,052	28,7				
MD_009,053	18,1				
MD_009,054	1,5		3		
MD_009,055	7,1	7,6	6,5		4,3
MD_009,056	14,1	19,3			14,4
MD_009,057	4				
MD_009,058	11,8				
MD_009,059	11,5	9,5			
MD_009,060					
MD_009,061	7,3				
MD_009,062					
MD_009,063	16				
MD_009,064					
MD_009,065	9,3				
Average	**11,84**	**9,13**	**8,78**	**9,25**	**9,25**

FSH					
Row Labels	**1**	**2**	**3**	**4**	**5**
MD_001,001	3,73	1,74	2,11	7,44	4,37
MD_001,002	1,86	7,07	3,75	3,31	7,62
MD_001,003	3,18	2,64	11,9	2,98	4,2
MD_001,004	5,64	6,32	4,55	6,13	3,93
MD_001,005	4,43	4,49	6,64	4,75	6,39
MD_001,006	4,78	5,15	4,78	4,13	5,51
MD_001,007	6,08	7,31	8,92	9,45	6,96
MD_001,008	4,8				
MD_001,009	2,51	2,88	4,25	2,55	6,99
MD_001,010	6,68	6,61	6,07	5,41	2,11
MD_001,011	8,24				
MD_001,012	5,45	4,63	3,75	3,74	3,63
MD_001,013	4,9	7,23	3,13		
MD_001,014	5,88				
MD_001,015	7,68	5,37	5,1	4,33	8,85
MD_001,016	6,48	4,67	7,49	4,55	5,7
MD_001,017	4,49	6,72	8,54	5,8	7,13
MD_001,018	2,23	7,98	3,83	4,93	4,39
MD_001,019	6,92	8,58	5,29	4,95	3,8
MD_001,020	4,49	7,36	8,16	6,43	1,24
MD_001,021	9,47	6,84			
MD_001,022	14,7				
MD_001,023	6,34	3,91	7,98	7,73	6,07
MD_001,024	17,9	6,09	3,41	5,04	5,51
MD_001,025	4,39	6,11	6,39	5,89	7,08
MD_001,026	5,55	9,98	1,66	6,99	6,07
MD_001,027	2,7	4,77	3,47	7,13	7,8
MD_001,028	6,9	4,06	14	1,88	5,48
MD_001,029	2,05	8,37	4,1	3,78	3,84
MD_001,030	3,38	7,82	6,37	4,4	8,26
MD_001,031	5,79				
MD_001,032	2,76	2,51	6,25	4,74	2,62
MD_001,033	10,4		4,77	8,85	6,76
MD_001,034	6,42				
MD_001,035	2,65	4,06	2,32	3,84	3,4
MD_001,037	4,46	5,03	4,72	3,21	2,6
MD_001,038	4,66	4,1	3,89	3,47	3,28
MD_001,039	2,61	6,67	4,06	10,2	9,77
MD_001,040	5,79	2,64	1,01	18,3	5,5
MD_001,041	5,72	7,88	6,43	3,63	3,34
MD_001,042	5,33	4,38	4,05	7,5	2,49
MD_001,043	6,33		5,51	3,85	3,71
MD_001,044	4,16	3,31	5,51	8,11	1,51
MD_001,045	2,78	4	3,06		
MD_001,046	4,45	4,45	4,43	1,88	3,48
MD_001,047	7,33	5,06	5,1	4,1	
MD_001,048	5,27	3,33	8,07	2,67	
MD_001,049	4,89	3,31	4,27		
MD_001,050	2,77	4,77		7,72	9,19
MD_001,051	4,17	4,39	9,32		
MD_001,052	7,45	8,5	8,25		
MD_001,053	5,27	3,91	1,52	4,73	
MD_001,054	4,31	18,3	9,8		
MD_001,055	1,79		3,83		
MD_001,056	4,68	4,86	7,16	8	
MD_001,057	5,89		6,56		
MD_001,058	7,73		3,48		
MD_001,059	6,49	8,62	5,81	6,44	
MD_001,060	8,23	4,86	5,48	4,82	
MD_001,061	2,96	3,67	3,18		
MD_001,062	7,99	6,98	5,44		
MD_001,063	6,6	4,67			
MD_001,064	8,4	6,76	2,7		
MD_001,065	2,11	2,62	5,12		
MD_001,066	6,33	5,57	9,22		
MD_001,067	6,22				
MD_001,068	3,95		2,59		
MD_001,069	1,48				
MD_001,070	6,7				
MD_001,071	4,05				
MD_001,072	4,25				
MD_001,073	3,08				
MD_001,074	5,96	5,38			
MD_001,075	5,98	8,46			
MD_001,076	5,1	2,01			
MD_001,077	3,64	1,94			
MD_001,078	4,87				
MD_001,080	8,11	11,6			
MD_001,081	4,31	6,54			
MD_001,082	8,26	3,46			
MD_001,083	3,85	5,19			
MD_001,084	5,72	7,09			
MD_001,085	5,56	4,89			
MD_001,086	7,87				
MD_001,087	6,27				
MD_001,088	5,76				
MD_001,089	16,3				
MD_001,090	1,93	4,91			
MD_001,092	5,48				
MD_001,093	4,71	5,19			
MD_001,094	5,25				
MD_001,095	2,6				
MD_001,096	3,18				
MD_001,098	15,7				
MD_001,100	12,2				
MD_002,001	8,89				
MD_005,001	4,27	3,22			
MD_005,002					
MD_005,003					
MD_005,004	2,79				
MD_006,002	6,07	4,87	7,54	2,79	4,55
MD_006,003	4,15				
MD_006,004	5,47	4,24	3,24	1,48	4,89
MD_006,005	5,95	6,5	2,54	2,07	4,71
MD_006,006	3,86	5,06	6,33	3,84	3,26
MD_006,007	8,33				
MD_006,008	6,08	8,19			3,65
MD_006,009	5,77	3,76			
MD_006,010	11,7				3,18
MD_006,011	7,83				
MD_007,001	7,39	8,41			
MD_007,003	3,67				
MD_008,001					
MD_009,001	19,3	6,03		6,75	4,14
MD_009,002	7,92	6,58		3,44	
MD_009,003	11,4		8,41		
MD_009,004	25,8				
MD_009,005	2,77	5,62		4,43	4,45
MD_009,006	6,51		7,36		
MD_009,007	5,76	5,77		8,61	6,43
MD_009,008	4,5	7,3		5,02	5,03
MD_009,009	4,22	4,52		5,83	6,65
MD_009,010	4,23	3,83		3,28	5,98
MD_009,011	3,19	8,53			
MD_009,012	9,43		4,36		
MD_009,013	2,42	3,79		4,92	5,02
MD_009,014	5,77	5,77			3,8
MD_009,015	10,8			1,86	
MD_009,016	2,86	2,39			
MD_009,017	6,36	4,63			
MD_009,018	6,82	2,69		8,03	2,99
MD_009,019	7,98				
MD_009,020	5,49	4,84		14,9	4,76
MD_009,021	5,62				
MD_009,022	3,8		5,73	2,7	4,46
MD_009,023	3,13		3,8		
MD_009,024	12,7	14	6,97		3,72
MD_009,025	4,5		17,1	5,51	3,32
MD_009,026	6,5				
MD_009,027	3,56	5,4	4,72		9,66
MD_009,028	3,17				
MD_009,029	1,36		3,29		
MD_009,030	3,88	4,84			
MD_009,031	5,61	4,37		3,01	15,3
MD_009,032	6,1	6,07		4,28	3,3
MD_009,033	1,91	6,67			
MD_009,034	7,1				
MD_009,035	7,62	8,27			
MD_009,036	3,62	3,84			
MD_009,037	4,61				
MD_009,038	8,76		5,08		
MD_009,039	7,34	4,24		7,73	
MD_009,040	7,66	2,86		7,01	
MD_009,041	5,54	3,92	5,55		
MD_009,042	3,51		9,79		
MD_009,043	2,24				
MD_009,044	9,79				
MD_009,045	5,33	4,9	4,31		
MD_009,046	5,29	2,42	3,45		
MD_009,047	8,84		4,84		
MD_009,048	3		10,4		
MD_009,049	5,12	2,25			3,78
MD_009,050	2,64		4,49		
MD_009,051	6,7	7,89	7,37		
MD_009,052	12				
MD_009,053	7,08				
MD_009,054			1,81		
MD_009,055	4,72	3,68	6,49		2,87
MD_009,056	6,64	6,81			4,73
MD_009,057	3,38				
MD_009,058	4,81				
MD_009,059	3,36	3,6			
MD_009,060					
MD_009,061	2,56				
MD_009,062					
MD_009,063	6,03				
MD_009,064	3				
MD_009,065	3,95				
Average	**5,85**	**5,50**	**5,60**	**5,43**	**5,08**

progesterone					
visit	**Baseline**	**2**	**3**	**4**	**5**
MD_001,001	0,079	11,9	1,91	0,953	0,05
MD_001,002	12	0,298	0,05	0,25	0,202
MD_001,003	3,83	11,8	0,05	11,1	0,098
MD_001,004	0,082	0,18	0,151	0,278	3,44
MD_001,005	0,169	0,114	0,05	2,76	0,05
MD_001,006	0,064	0,136	0,05	0,094	0,05
MD_001,007	0,145	2,47	0,107	0,516	1,81
MD_001,008	6,95				
MD_001,009	2,74	11,4	0,268	1,04	11
MD_001,010	9,49	0,087	1,48	6,43	5,86
MD_001,011	0,251				
MD_001,012	0,324	0,366	0,261	0,287	0,006
MD_001,013	1,65	0,062	7,04		
MD_001,014	0,05				
MD_001,015	0,114	0,308	0,053	0,251	1,71
MD_001,016	6,17	12,4	0,16	14,1	11,1
MD_001,017	21,6	0,377	0,125	0,254	0,089
MD_001,018	10,4	0,445	0,159	0,324	0,524
MD_001,019	0,078	0,344	0,245	0,106	0,05
MD_001,020	0,225	0,05	0,178	0,05	2,27
MD_001,021	0,834	0,103			
MD_001,022	0,925				
MD_001,023	0,423	8,54	0,053	0,131	0,097
MD_001,024	0,547	0,259	0,05	0,246	0,05
MD_001,025	0,151	0,125	0,094	0,2	0,05
MD_001,026	0,179	0,364	0,142	0,233	0,097
MD_001,027	0,087	6,81	19,2	0,162	1,52
MD_001,028	0,693	0,002	0,258	0,076	5,48
MD_001,029	1,6	0,43	0,136	0,984	0,255
MD_001,030	9,35	0,15	0,11	0,05	0,583
MD_001,031	0,161				
MD_001,032	20,6	20,5	1,56	0,05	10,7
MD_001,033	0,107		0,095	1,71	0,162
MD_001,034	0,06				
MD_001,035	20,5	15,2	17,6	0,255	15,5
MD_001,037	14,2	12,2	19,7	0,165	14,3
MD_001,038	0,113	0,136	0,153	0,125	0,165
MD_001,039	21,4	0,212	17,9	0,077	0,843
MD_001,040	0,105	0,276	0,289	0,05	0,235
MD_001,041	1,91	0,323	0,05	0,006	0,271
MD_001,042	0,55	0,273	0,081	0,843	3,73
MD_001,043	0,099		0,05	0,797	1,5
MD_001,044	0,05	0,25	0,05	0,167	10,6
MD_001,045	23,7	0,148	0,461		
MD_001,046	3,76	0,516	0,05	0,076	0,298
MD_001,047	0,138	0,135	0,183	0,361	
MD_001,048	0,167	0,246	0,967	9,47	
MD_001,049	6,34	0,006	23,6		
MD_001,050	13,2	0,128		0,327	0,114
MD_001,051	0,573	2,97	0,083		
MD_001,052	0,129	0,131	0,222		
MD_001,053	0,179	0,337	10,9	0,274	
MD_001,054	8,89	0,05	0,05		
MD_001,055	0,487		0,321		
MD_001,056	1,29	6,06	0,306	0,538	
MD_001,057	0,2		0,076		
MD_001,058	0,131		1,78		
MD_001,059	0,319	0,119	0,416	0,193	
MD_001,060	0,05	0,606	0,29	0,459	
MD_001,061	0,127	0,265	11,1		
MD_001,062	0,578	0,546	0,562		
MD_001,063	0,205	0,329			
MD_001,064	0,05	0,162	14,1		
MD_001,065	5,86	10,7	0,139		
MD_001,066	0,075	0,131	0,412		
MD_001,067	1,61				
MD_001,068	5,3		7,7		
MD_001,069	8,05				
MD_001,070	1,45				
MD_001,071	0,106				
MD_001,072	0,066				
MD_001,073	16,1				
MD_001,074	0,238	0,204			
MD_001,075	0,554	0,273			
MD_001,076	0,183	11,5			
MD_001,077	0,218	4,84			
MD_001,078					
MD_001,080	0,167	0,406			
MD_001,081	15,2	1,35			
MD_001,082	0,583	5,53			
MD_001,083	0,797	0,091			
MD_001,084	1,71	0,28			
MD_001,085	0,117	0,094			
MD_001,086	0,246				
MD_001,087	0,288				
MD_001,088	11,6				
MD_001,089	0,129				
MD_001,090	0,328	0,1			
MD_001,092	0,298				
MD_001,093	2,45	0,332			
MD_001,094	0,397				
MD_001,095	0,143				
MD_001,096	11,1				
MD_001,098	0,889				
MD_001,100	0,849				
MD_002,001	0,066				
MD_005,001	14,3	8,6			
MD_005,002					
MD_005,003	0,094				
MD_005,004	10,6				
MD_006,002	0,101	10,5	0,139	0,149	
MD_006,003	21,3				
MD_006,004	0,104	0,55	0,116	18,8	0,481
MD_006,005	0,074	0,04	1,11	1,82	0,2
MD_006,006	20,5	12,7	0,255	0,162	0,165
MD_006,007	0,05				
MD_006,008	0,436	0,408			14,3
MD_006,009	13,4	6,74			
MD_006,010	0,691				6,38
MD_006,011	0,205				
MD_007,001	5,86	0,242			
MD_007,003	0,05				
MD_008,001					
MD_009,001	0,726	0,138		0,357	10,1
MD_009,002	0,226	0,109		6,84	
MD_009,003	0,898		0,487		
MD_009,004	0,074				
MD_009,005	8,17	3,95		5	0,068
MD_009,006	0,11		3,51		
MD_009,007	2,09	9,26		1,02	0,461
MD_009,008	14,8	13,2		0,071	20,6
MD_009,009	0,112	5,19		15,2	0,466
MD_009,010	19	19		17	0,318
MD_009,011	12,3	0,139			
MD_009,012	0,535		6,15		
MD_009,013	17,3	6,55		8,89	0,269
MD_009,014	0,12	8,95			15,9
MD_009,015	0,47			18,9	
MD_009,016	14,6	11,4			
MD_009,017	13,1	11,8			
MD_009,018	0,169	24,2		0,185	2,71
MD_009,019	0,705				
MD_009,020	0,313	11		0,468	3,68
MD_009,021	0,131				
MD_009,022	4,23		0,226	8,21	0,233
MD_009,023	14,9		8,28		
MD_009,024	0,841	0,782	0,235		6,55
MD_009,025	7,95		0,916	0,145	12,4
MD_009,026	0,156				
MD_009,027	12,2	0,353	5,36		1,36
MD_009,028	12,1				
MD_009,029	0,073		16,1		
MD_009,030	0,17	0,325			
MD_009,031	0,219	0,197		0,234	0,875
MD_009,032	0,247	10		0,218	9,31
MD_009,033	14,8	1,32			
MD_009,034	0,515				
MD_009,035	0,197	0,068			
MD_009,036	0,05	2,35			
MD_009,037	15,5				
MD_009,038	0,598		10,6		
MD_009,039	0,093	0,141		0,378	
MD_009,040	0,139	9,51		0,272	
MD_009,041	0,336	2,83	0,441		
MD_009,042	2,23		0,711		
MD_009,043	0,349				
MD_009,044	0,191				
MD_009,045	0,071	9,8	0,239		
MD_009,046	0,286	13,2	4,54		
MD_009,047	0,331		0,332		
MD_009,048	17,4		0,359		
MD_009,049	0,05	14,3			0,162
MD_009,050	11,4		0,263		
MD_009,051	0,05	0,161	0,072		
MD_009,052	0,24				
MD_009,053	0,237				
MD_009,054	0,259		0,344		
MD_009,055	0,05	0,203	0,239		18,3
MD_009,056	0,052	0,262			0,28
MD_009,057	15,9				
MD_009,058	0,165				
MD_009,059	2,66	2,64			
MD_009,060	0,616				
MD_009,061	6,47				
MD_009,062					
MD_009,063	0,071				
MD_009,064	0,219				
MD_009,065	15,7				
Average	3,87	3,78	2,77	2,52	3,78

Estradiol levels					
Visit	**1**	**2**	**3**	**4**	**5**
MD_001,001	37,3	290	67,8	430	27,7
MD_001,002	262	73,4	43,1	64,2	36,1
MD_001,003	109	329	62,5	125	117,9
MD_001,004	73,7	51,4	43,2	37	60,4
MD_001,005	344	79,1	382	96,6	64,8
MD_001,006	98	27,8	27	26,5	29,6
MD_001,007	61,9	128	38,2	30,8	97
MD_001,008	127				
MD_001,009	50,1	174	138	139	121
MD_001,010	73,5	31,7	184	120	137
MD_001,011	25,4				
MD_001,012	105	94,9	148	279	98,9
MD_001,013	33,5	33,5	113		
MD_001,014	37,4				
MD_001,015	37,4	71,3	101,4	27	182
MD_001,016	85	132	142	220	127
MD_001,017	209	141	62,6	345	83,5
MD_001,018	133	70	185	83,8	43,3
MD_001,019	32,7	29,8	66,5	87,2	117
MD_001,020	242	63,1	88,7	78,5	78,4
MD_001,021	326	44,2			
MD_001,022	138				
MD_001,023	525	152	54,7	107	49,7
MD_001,024	61,4	30	160	83,4	92
MD_001,025	89	64,4	90,4	72,8	69,4
MD_001,026	118	64,1	536	69,5	49,7
MD_001,027	417	228	379	120	118
MD_001,028	80,1	142	46,5	55,5	107
MD_001,029	286	45	49	58,4	57,7
MD_001,030	123	45,7	51,3	50	51,4
MD_001,031	37,2				
MD_001,032	280	541	53,6	513	136
MD_001,033	50		139	139	77,6
MD_001,034	29,7				
MD_001,035	244	142	233	577	145
MD_001,037	156	123	127	234	175
MD_001,038	56,1	49	45,1	60,7	59,9
MD_001,039	236	97,7	115	125	171
MD_001,040	27,1	50	50	45,7	75,7
MD_001,041	91,5	72,6	78,5	78,9	77,1
MD_001,042	225	298	39,3	171	147
MD_001,043	103		292	293	112
MD_001,044	195	196	192	192	220
MD_001,045	195	98	45		
MD_001,046	50,6	50,8	58,5	58,5	57,9
MD_001,047	57	72,1	104,8	105	
MD_001,048	52,9	285	484	95,4	
MD_001,049	87,1	187	158		
MD_001,050	117	118		43,2	60,5
MD_001,051	424	105	95,9		
MD_001,052	50,8	50,1	41,6		
MD_001,053	88,6	100,1	144	78,2	
MD_001,054	133	135,7	97,5		
MD_001,055	46,1		143		
MD_001,056	42	81,4	57,1	55,3	
MD_001,057	72,8		85,4		
MD_001,058	107		192		
MD_001,059	415	33,4	72,1	89,1	
MD_001,060	78,7	81,4	107	115	
MD_001,061	100,4	397	321		
MD_001,062	61,4	75,6	40,4		
MD_001,063	68,1	50,2			
MD_001,064	66,3	47,6	237		
MD_001,065	137	136	87,1		
MD_001,066	66	64,1	68,7		
MD_001,067	75,9				
MD_001,068	519		416		
MD_001,069	147				
MD_001,070	68,4				
MD_001,071	105				
MD_001,072	51,6				
MD_001,073	138				
MD_001,074	38,9	149			
MD_001,075	50,9	34,3			
MD_001,076	44,8	189			
MD_001,077	94,4	213			
MD_001,078	186				
MD_001,080	56,6	55,7			
MD_001,081	153	127			
MD_001,082	300	114			
MD_001,083	113	54,4			
MD_001,084	97,6	113			
MD_001,085	264	75,9			
MD_001,086	61,3				
MD_001,087	118				
MD_001,088	206				
MD_001,089	50,3				
MD_001,090	80	39,6			
MD_001,092	50,9				
MD_001,093	52	57,7			
MD_001,094	429				
MD_001,095	175				
MD_001,096	321				
MD_001,098	259				
MD_001,100	378				
MD_002,001	220				
MD_005,001	154	293			
MD_005,002					
MD_005,003					
MD_005,004	215				
MD_006,002	47,8	120		69,4	208
MD_006,003	187				
MD_006,004	74,7	70,5	45	201	26,9
MD_006,005	47	52,1	55,1	97,8	
MD_006,006	159	82,4	35,6		163
MD_006,007	39,8				
MD_006,008		229			239
MD_006,009	218	227			
MD_006,010	91				171
MD_006,011					
MD_007,001	92,4	43,4			
MD_007,003	26,5				
MD_008,001					
MD_009,001	127			267	66,4
MD_009,002	52	77,2		93,3	
MD_009,003	322		52,6		
MD_009,004	90,4				
MD_009,005	170	69,6		89,5	173
MD_009,006	36,2		49,6		
MD_009,007	55,6	63		120	79,9
MD_009,008	220	169		255	207
MD_009,009	180	58,4		110	41,8
MD_009,010	62,8	83,2		81,1	38,1
MD_009,011	163	61,9			
MD_009,012	177		60		
MD_009,013	365	166		416	105
MD_009,014	78,4	126			208
MD_009,015	194			118	
MD_009,016	117	105			
MD_009,017	141	288			
MD_009,018	34,8	213		70,9	71
MD_009,019	92,3				
MD_009,020	92,9	120		298	82,9
MD_009,021					
MD_009,022	79,7		47	118	57,3
MD_009,023	190		117		
MD_009,024	253	250	45,3		91,1
MD_009,025	150		290	164	263
MD_009,026	45,1				
MD_009,027	197	87,8	217		260
MD_009,028	204				
MD_009,029			222		
MD_009,030					
MD_009,031					418
MD_009,032	377	103		209	157
MD_009,033	309	199			
MD_009,034	51,2				
MD_009,035	51,9	34,3			
MD_009,036	209	75,3			
MD_009,037	179				
MD_009,038	380		146		
MD_009,039	43,7	171		69,9	
MD_009,040	57,8	267		111	
MD_009,041	46,8	119	59,1		
MD_009,042	64,8		130		
MD_009,043					
MD_009,044	79,9				
MD_009,045	167	124	112		
MD_009,046	437	173	89,1		
MD_009,047	73,5				
MD_009,048	159		56,9		
MD_009,049	167	156			260
MD_009,050	309		237		
MD_009,051	107		41		
MD_009,052	263				
MD_009,053	492				
MD_009,054					
MD_009,055	130	391	37,4		162
MD_009,056	39,5	66,5			229
MD_009,057	182				
MD_009,058	59,7				
MD_009,059	80,8	91,3			
MD_009,060					
MD_009,061	111				
MD_009,062					
MD_009,063	82,9				
MD_009,064					
MD_009,065	128				
Average	143,74	122,98	125,96	142,49	119,83

26. STUDY RESULTS: LIVER FUNCTION

Blood samples to measure haemoglobin, bilirubin, ALAT, ASAT, were done in the local laboratories at screening, months 3, 6, 9 and 12 or until normalisation of the values. Generally, reference ranges for Alanine transaminase (ALAT): < 35 IU/L, for Aspartate transaminase (ASAT): <35 IU/L, for total bilirubin: 5-21 umol/l and for haemoglobin: 11.7-15.5 g/dL.

DILI was defined as alanine aminotransferase (ALT) > 5-fold the upper limit of normal (5× ULN), alkaline phosphatase (ALP) > 2× ULN, or ALT > 3× ULN and total bilirubin > 2× ULN. Hy' law was defined as DILI resulting in increased ALT > 3× ULN and total bilirubin > 2× ULN after excluding other potential causes and without a significant cholestatic component (ALP > 2× ULN).[16]

If the participant develops transaminase levels more than 3 times the upper limit of normal, or the bilirubin more than 2 times the ULN the participant will be withdrawn from the treatment and shall be monitored closely.[5] Liver tests should be repeated weekly after stopping treatment. For any participant with signs or symptoms consistent with liver injury (such as nausea, vomiting, right hypochondrial pain, anorexia, asthenia, jaundice), transaminase levels will be checked immediately. In case of results between 2 and 3 times the ULN for ASAT or ALAT, or above ULN and lower than 2 times the ULN for bilirubin, a monthly control of liver function will be advised.
In case of elevation of ALAT or ASAT more than 3 times the ULN or bilirubin more than 2 times the ULN, or developing severe hypertension, medication must be stopped.

Bilirubin, ASAT and ALAT:

Bilirubine						**ALAT**						**ASAT**					
Visit number	1	2	3	4		Visit number	1	2	3	4	5	Visit number	1	2	3	4	5
N	174	107	81	63	62	N	174	107	81	63	62	N	174	107	81	64	63
Average	11,01	10,23	11,04	10,35	12,13	Average	15,69	14,41	15,95	16,85	15,82	Average	20,64	20,57	19,69	19,86	21,07

5 (4,7%) of the 106 participants had a slightly elevated (< than 1,5 times UNL) bilirubin at one of the follow up visits. One (1,9%) of the participants had mildly elevated (< than 2 or 3 times UNL) bilirubine at the last follow up visit.
9 (8,4%) of the 106 participants developed a slightly elevated ALAT (less than 2 times ULN)
4 (3,8%) of the participants developed a slightly increased ASAT (< than 2 times UNL) and 1 (1%) an mildly elevated ASAT (2-3 times ULN) at one of the follow up visits.

Participant MD_009.056, a 21 year old women had increased liver functions at visit 5.
Bilirubine of 49 (2-3 times ULN) and ASAT 119.6 (3- 5 times ULN): and ALAT 53.0, Value between 1.0-2.0 ULN. On July 4 2024 a new blood test was done and liver values had almost normalized, ALAT 9,8 UL, ASAT 15.93 UL and bilirubin 38,11.
The participants was send for a hepatological consultation. More information will be shared in the next report.

This case might be a Hy's Law case [6] which is essentially a translation of Zimmerman's observation that pure hepatocellular injury sufficient to cause hyperbilirubinemia is an ominous indicator of the potential for a drug to cause serious liver injury. Thus, a finding of ALT elevation, usually substantial, seen concurrently with bilirubin >2xULN, identifies a drug likely to cause severe DILI (fatal or requiring transplant) at a rate roughly 1/10 the rate of Hy's Law cases.
Hy's Law cases have the following three components:

- The drug causes hepatocellular injury, generally shown by a higher incidence of 3-fold or greater elevations above the ULN of ALT or AST than the (nonhepatotoxic) control drug or placebo
- Among trial subjects showing such AT elevations, often with ATs much greater than 3xULN, one or more also show elevation of serum TBL to >2xULN, without initial findings of cholestasis (elevated serum ALP)
- No other reason can be found to explain the combination of increased AT and TBL, such as viral hepatitis A, B, or C; preexisting or acute liver disease; or another drug capable of causing the observed injury.

Finding one Hy's Law case in the clinical trial database is worrisome; finding two is considered

highly predictive that the drug has the potential to cause severe DILI when given to a larger population.[7]

Visit number	1	2	3	4	5
MD_001_001	8,2	5,9	10,4	9,5	5,9
MD_001_002	7,9	13,8	11,3	20,5	5,9
MD_001_003	11,9	11,2	8	8,1	6,1
MD_001_004	5,2	7,5	4,5	6,7	6,3
MD_001_005	11,5	12,4	9,3	10,3	6,6
MD_001_006	5,9	5,6	7,8	5,9	6,7
MD_001_007	9,2	8,7	7,9	5,9	6,9
MD_001_008	9,4				7,1
MD_001_009	6,9	8,5	7,6	7,5	7,1
MD_001_010	11,3	8,2	12,4	7,8	7,2
MD_001_011	7,7				7,6
MD_001_012	13,9	14,1	17,5	20,2	7,6
MD_001_013	6,8	10,9	15		7,9
MD_001_014	7,5				8,1
MD_001_015	10,4	7,5	6,7	8,1	8,4
MD_001_016	6,3	7,7	9,4	7,8	8,4
MD_001_017	20,1	18,5	24,6	20,9	8,5
MD_001_018	14,3	5	7,7	8,2	8,6
MD_001_019	4,8	7,2	5,9	9,2	8,8
MD_001_020	20,7	6,8	7	10,1	8,9
MD_001_021	15,5	11,7			8,9
MD_001_022	13,4				8,9
MD_001_023	8,3	7,5	12,2	8,7	8,9
MD_001_024	9,4	5,7	13,6	10,5	8,9
MD_001_025	8,8	11,5	18,3	15,6	9,3
MD_001_026	10,9	12,8	17,5	9,8	9,6
MD_001_027	6,6	7,1	13,6	9,5	9,7
MD_001_028	8,1	12,3	18,8	20,3	9,8
MD_001_029	11,2	8,4	6,7	13,5	10,3
MD_001_030	18,1	13,1	18	10,3	10,4
MD_001_031	7,3				10,7
MD_001_032	17,1	8,9	15,4	9,2	10,8
MD_001_033	8,9		10,2	12,7	11,2
MD_001_034	7,3				11,4
MD_001_035	12,4	12,3	20,6	17,9	11,5
MD_001_037	13,2	11,6	9,7	9,5	12,6
MD_001_038	5,7	6,7	5,8	6,9	12,7
MD_001_039	8,6	5,2	9,2	6,8	12,8
MD_001_040	26,1	7,9	7,5	11	12,9
MD_001_041	5,6	5,3	10,1	12,6	13,4
MD_001_042	11,6	15,6	14,8	8,6	13,6
MD_001_043	25,5		20,7	8,6	13,7
MD_001_044	8,2	20,2	10,7	8,8	13,8
MD_001_045	12,6	8,3	14,5		14,1
MD_001_046	13,2	5,9	10,1	20,3	14,2
MD_001_047	9,4	6,2	17	8,5	14,2
MD_001_048	4,8	6,6	6,5	8,3	14,7
MD_001_049	20,4	19,1	15,1		15
MD_001_050	12,7	10,6		5,5	15,2
MD_001_051	8	9,5	7,3		15,3
MD_001_052	7,9	9,4	7,7		15,5
MD_001_053	4,7	8,8	7,5	8,2	15,5
MD_001_054	11,7	11	11,4		15,8
MD_001_055	11,2		8,6		15,8
MD_001_056	7,4	8,2	6,4	8,3	16
MD_001_057	15,6		10,7		16,3
MD_001_058	8,7		8,4		16,7
MD_001_059	11,4	9	13	11,4	16,9
MD_001_060	11	8,2	18,9	7,7	17,9
MD_001_061	4,7	5,6	7,7		18,9
MD_001_062	11,6	9,7	10,4		20,4
MD_001_063	16,3	5,7			21,8
MD_001_064	20,4	15	15,3		
MD_001_065	8,9	14,8	5,1		
MD_001_066	7,5	8,2	8,8		
MD_001_067	19,4				
MD_001_068	8,1		7,9		
MD_001_069	8,4				
MD_001_070	13,8				
MD_001_071	12				
MD_001_072	4,1				
MD_001_073	12,2				
MD_001_074	18,8	16,8			
MD_001_075	12,2	13,1			
MD_001_076	17	14,1			
MD_001_077	5,5	9,6			
MD_001_078	3,8				
MD_001_080	8,8	9,7			
MD_001_081	12,4	13,6			
MD_001_082	16,3	8			
MD_001_083	8,6	8,6			
MD_001_084	9,7	10,8			
MD_001_085	9,4	8,4			
MD_001_086	11				
MD_001_087	10,4				
MD_001_088	10,4				
MD_001_089	9,4				
MD_001_090	11,6	12,4			
MD_001_092	5,4				
MD_001_093	7,7	9,6			
MD_001_094	14,1				
MD_001_095	16,7				
MD_001_096	11,8				
MD_001_098	15,7				
MD_001_100	16,9				
MD_002_001	6,5				
MD_005_001	7,7	12,7			
MD_005_002					
MD_005_003	6,4				
MD_005_004	13,2				
MD_006_002	5,3	8,1	3,9	9,4	
MD_006_003	6				
MD_006_004	9,3	6,3	9,1	6,8	
MD_006_005	23	22,4	26,8	20,3	
MD_006_006	5,9	5,3	7,3	4,9	
MD_006_007	11				
MD_006_008	5,4	9,9			
MD_006_009	11,2	5,5			
MD_006_010	10,1				
MD_006_011	10,7				
MD_007_001	12,5	15,2			
MD_007_003	14,5				
MD_008_001					
MD_009_001	9,9	7,5		5	
MD_009_002	12	10,1		7,7	
MD_009_003	14,7		12,8		
MD_009_004	14,6				
MD_009_005	12,1	6,1		9,8	
MD_009_006	11,3		9,3		
MD_009_007	10,5	12,2		9,6	
MD_009_008	8,4	9,1		9,2	
MD_009_009	18,2	17		10,6	
MD_009_010	6	8,1		11,9	
MD_009_011	9,9	8,9			
MD_009_012	5,2		9,2		
MD_009_013	10	6,7		7,7	
MD_009_014	23,2	11,1			
MD_009_015	6,9			9,1	
MD_009_016	11,1	7			
MD_009_017	12,6	11,1			
MD_009_018	12,9	12,8		11,5	
MD_009_019	7,9				
MD_009_020	16,6	9		19,5	
MD_009_021	6,6				
MD_009_022	8,7		10,7	8	
MD_009_023	15,9		6		
MD_009_024	9,6	15,8	9,2		
MD_009_025	8,1		13,8	8,5	
MD_009_026	13				
MD_009_027	19,9	17,4	20,2		
MD_009_028	12				
MD_009_029	6,5		7,1		
MD_009_030	10,3	6,9			
MD_009_031	6,7	6,2		11,4	
MD_009_032	11	14,1		9,2	
MD_009_033	8,9	9,9			
MD_009_034	16,8				
MD_009_035	12,1	9,2			
MD_009_036	8	7,5			
MD_009_037	6,4				
MD_009_038	12,7		11,8		
MD_009_039	14,4	11,6		11,5	
MD_009_040	7,6	7,6		5,1	
MD_009_041	8,7	9,8	4,2		
MD_009_042	7,7	6,3	6,6		
MD_009_043	5,2				
MD_009_044	11,2				
MD_009_045	9,6	11,4	9,4		
MD_009_046	11,2	9,5	9,2		
MD_009_047	11,3		8,3		
MD_009_048	8,6		9,6		
MD_009_049	21,1	16,6			
MD_009_050	10,3		18,4		
MD_009_051	10,4	8,1	7,1		
MD_009_052					
MD_009_053	19				
MD_009_054	6,6		8,6		
MD_009_055	12,7	15,3	10,7		
MD_009_056	25,3	23		49,4	
MD_009_057	16,9				
MD_009_058	9,7				
MD_009_059	11,3	8,5			
MD_009_060	9,3				
MD_009_061	12,5				
MD_009_062					
MD_009_063	5,7				
MD_009_064	5				
MD_009_065	8,4				
Average	11,01	10,23	11,04	10,35	11,53

Visit number	1	2	3	4	5
MD_001_001	27,2	21,4	19,2	18,6	14,5
MD_001_002	9,4	8,2	17,3	7	23,1
MD_001_003	18,5	29,9	58	32,6	14
MD_001_004	20,6	25,9	15,8	25	24,4
MD_001_005	8,6	9,5	9	9,7	9
MD_001_006	32,4	42,2	31,6	33,5	25,4
MD_001_007	12,9	10,5	10,1	11	13,6
MD_001_008	13,7				
MD_001_009	14,1	12,4	13,4	19,1	14,7
MD_001_010	16,8	31,7	7,6	23,4	6,8
MD_001_011	27,7				
MD_001_012	20,6	15,9	18,7	15,9	28,8
MD_001_013	8,6	10,3	11		
MD_001_014	27,1				
MD_001_015	17,4	41,5	24,9	12,3	16
MD_001_016	8	8,6	7	7,3	5,6
MD_001_017	19,3	23,6	13,9	12,4	17
MD_001_018	10,5	11,1	14,9	12	10,5
MD_001_019	11,4	12,5	13,3	14,7	12,3
MD_001_020	11,6	38	33,7	20,4	12,6
MD_001_021	9,3	9			
MD_001_022	18,8				
MD_001_023	13,3	9,5	12,1	12	16,5
MD_001_024	12,8	14,2	19,8	34,1	14
MD_001_025	12	32,4	12,8	34,5	8,1
MD_001_026	13,1	12,5	13,7	12,9	16,5
MD_001_027	9,5	8,3	9,6	9,7	8,3
MD_001_028	19,7	21	13,1	11,3	16,7
MD_001_029	8,2	12,4	32,6	11,5	14
MD_001_030	16,2	10,6	12,8	17,9	13,1
MD_001_031	15				
MD_001_032	8,7	8,2	7,2	7,9	16,1
MD_001_033	8,8		13	16	14,5
MD_001_034	24,3				
MD_001_035	12,8	21	13,8	14	12,8
MD_001_037	23,7	15,2	22	20	6,7
MD_001_038	25,2	34,6	29,7	21,9	30,5
MD_001_039	11,3	11,4	27,5	18,4	19,3
MD_001_040	10,5	9,5	11	23,8	17,4
MD_001_041	20,3	34,6	20,4	28,8	20,9
MD_001_042	14	14	13,3	19,3	10,5
MD_001_043	12,6		14	17,2	23,4
MD_001_044	10,8	15,9	14	34,1	8
MD_001_045	13,8	26,3	15		
MD_001_046	15	11	20,4	11,3	17,5
MD_001_047	9,3	12,9	13,9	12	
MD_001_048	26,7	15,8	20,3	8,6	
MD_001_049	12,6	10,9	11,3		
MD_001_050	11,6	14,2		16	17,2
MD_001_051	22,3	19,3	19,8		
MD_001_052	16	18,8	12,9		
MD_001_053	32,4	13,8	16,4	20	
MD_001_054	15,3	23,8	14,7		
MD_001_055	9,6		7,5		
MD_001_056	19,8	25,7	19,9	19,4	
MD_001_057	34,5		11,5		
MD_001_058	12		11,4		
MD_001_059	18,7	20,1	9,1	8,5	
MD_001_060	17,4	25,7	16,7	11,3	
MD_001_061	10	27,9	12,9		
MD_001_062	12,6	10,6	10,1		
MD_001_063	9,8	13,2			
MD_001_064	14,9	14,5	14		
MD_001_065	6,8	16,1	11,9		
MD_001_066	18,9	17,3	14,3		
MD_001_067	10,7				
MD_001_068	12,4		16,8		
MD_001_069	10,1				
MD_001_070	18,1				
MD_001_071	14,2				
MD_001_072	25,5				
MD_001_073	25,5				
MD_001_074	12,7	13,5			
MD_001_075	12,4	33,7			
MD_001_076	13,9	15,3			
MD_001_077	10,3	10,5			
MD_001_078	27,1				
MD_001_080	34,1	13,6			
MD_001_081	10,2	11,3			
MD_001_082	13,1	15,9			
MD_001_083	17,2	26,5			
MD_001_084	11,8	13,2			
MD_001_085	10	21,4			
MD_001_086	15,3				
MD_001_087	8,2				
MD_001_088	11,4				
MD_001_089	18				
MD_001_090	18,3	21,1			
MD_001_092	15,3				
MD_001_093	24,4	16,6			
MD_001_094	10,5				
MD_001_095	6,7				
MD_001_096	20,1				
MD_001_098	15,4				
MD_001_100	19,3				
MD_002_001	11,8				
MD_005_001	32,8	21,1			
MD_005_002	12				
MD_005_003	15,5				
MD_005_004	18	-99			
MD_006_002	17,6	27,1	14,1	14,5	14,4
MD_006_003	8,9				
MD_006_004	14,8	23,4	28	41,5	17,1
MD_006_005	13,1	13,2	21	21,6	17,1
MD_006_006	11,6	13,6	10,7	12	12
MD_006_007	10,4				
MD_006_008	12	12,1			9,8
MD_006_009	11,9	11			
MD_006_010	17,5				39
MD_006_011	18,6				
MD_007_001	11,7	9,2			
MD_007_003	11,3				
MD_008_001					
MD_009_001	10,2	15,8		10,4	11,1
MD_009_002	17,4	13,6		11,5	
MD_009_003	16		13,7		
MD_009_004	11,1				
MD_009_005	10,7	9,8		10,3	8,2
MD_009_006	50,8		48,9		
MD_009_007	10,1	8,9		10,7	10,5
MD_009_008	19,8	12,6		14	10,8
MD_009_009	6,9	7,7		7,1	8,5
MD_009_010	10,5	11,4		12,5	12,1
MD_009_011	20,2	11,3			
MD_009_012	11,4		16,5		
MD_009_013	16,6	18,2		34,6	16,7
MD_009_014	14,1	11,5			44
MD_009_015	14,9			18,9	
MD_009_016	13,2	15,3			
MD_009_017	17,9	13,9			
MD_009_018	14,4	15,6		15	12,5
MD_009_019	14,1				
MD_009_020	9,8	8,7		9,9	10,3
MD_009_021	15,4				
MD_009_022	37,8		15,7	17,6	10,8
MD_009_023	7,7	0	10,3		
MD_009_024	9,3	11,7	10,5		11,8
MD_009_025	9,4		8,9	10,4	10,7
MD_009_026	12,8				
MD_009_027	11,1	12,2	14,5		12,9
MD_009_028	11,2				
MD_009_029	10,2		11,3		
MD_009_030	11,8	15,2			
MD_009_031	9,2	13,8		14	12,8
MD_009_032	18,9	13,5		16,2	13,5
MD_009_033	13,9	25,7			
MD_009_034	10,9				
MD_009_035	16,5	15,2			
MD_009_036	9,4	8,4			
MD_009_037	11,6				
MD_009_038	14,4		15,1		
MD_009_039	12,6	14,7		10,5	
MD_009_040	14,7	18,5		18,2	
MD_009_041	13,2	10,6	12		
MD_009_042	34,3	17,3	19,3		
MD_009_043	13,2				
MD_009_044	11,9				
MD_009_045	9,7	8	10,8		
MD_009_046	14,9	14,2	12,9		
MD_009_047	13,8		12		
MD_009_048	13,1		15,1		
MD_009_049	20,1	14,5			22,6
MD_009_050	12		11,3		
MD_009_051	11,4	15,2	9,1		
MD_009_052	15,2				
MD_009_053	14,4				
MD_009_054	10,3		10		
MD_009_055	9,9	9,1	7,8		11,1
MD_009_056	15	10,2			53
MD_009_057	15				
MD_009_058	21,5				
MD_009_059	23,3	17,5			13
MD_009_060	80,9				
MD_009_061	8,6				
MD_009_062					
MD_009_063	24,1				
MD_009_064	9,7				
MD_009_065	13				
Average	15,69	15,32	15,95	16,85	15,82

Visit number	1	2	3	4	5
MD_001_001	24,9	20,7	16,5	18	17,5
MD_001_002	19	16	29,9	15,1	21,9
MD_001_003	23,8	28,5	43,2	22,3	17,2
MD_001_004	16,4	36,1	18	22,4	22,8
MD_001_005	19,3	19,5	18,5	19	17,8
MD_001_006	20,1	30,8	23,3	27	24,5
MD_001_007	15,9	13,4	11,7	12,3	12
MD_001_008	20,1				
MD_001_009	17,4	17,3	16,7	21,8	14,7
MD_001_010	33,7	28	14,4	16,1	12,4
MD_001_011	24,2				
MD_001_012	22,7	17,7	20,9	21,2	32,7
MD_001_013	12,9	14,2	15,7		
MD_001_014	21,3				
MD_001_015	21,7	34,5	19,8	20,8	26,2
MD_001_016	16,1	18,7	17,7	17,4	16,8
MD_001_017	21	29,8	21,1	18,9	22,1
MD_001_018	14,3	23,3	15,1	16,6	15,8
MD_001_019	18	19	19,5	20,4	19,2
MD_001_020	14,6	32	33,5	17,8	24,8
MD_001_021	12,7	18,3			
MD_001_022	34,3				
MD_001_023	18,3	18,5	21,4	24,1	24
MD_001_024	21,7	16,4	18,4	22,3	14,7
MD_001_025	17,8	36,9	18,2	32,1	16,1
MD_001_026	22,2	19,5	21,3	25,8	24
MD_001_027	14,7	10,6	14,9	12,6	14
MD_001_028	20,7	22,3	17	17,6	27
MD_001_029	14,5	15,4	24,4	15,8	20,8
MD_001_030	17,8	15,3	16,9	19,9	16,9
MD_001_031	20,2				
MD_001_032	16	25	15,4	15,1	25
MD_001_033	18,6		23,7	26,2	17,5
MD_001_034	28,3				
MD_001_035	18,7	22,3	20,9	20,8	18,6
MD_001_037	42,5	19,5	24,4	21,4	17,9
MD_001_038	24,2	24,4	22	18,8	21,8
MD_001_039	22,6	19,4	30,4	19,7	23
MD_001_040	13,3	15,4	15,5	23,3	20,4
MD_001_041	19,1	26	17,8	32,7	17,4
MD_001_042	19,4	17,7	17,3	23	15,5
MD_001_043	19,7		20,7	14,7	27,8
MD_001_044	17,1	21,2	14,7	32,1	22
MD_001_045	19,6	27,6	29		
MD_001_046	23,9	12,3	17,8	17,6	18,4
MD_001_047	14,3	16,9	14,9	16,1	
MD_001_048	33,6	17,8	22,1	14,9	
MD_001_049	25,3	16,5	21,2		
MD_001_050	16,7	14,7		18,1	18,9
MD_001_051	17,1	22,7	21,2		
MD_001_052	14	27,7	16,3		
MD_001_053	33,3	19,7	17,1	18,2	
MD_001_054	20,8	23,3	16,8		
MD_001_055	11,8		13,7		
MD_001_056	21,8	28,8	28	21,9	
MD_001_057	32,1		17,4		
MD_001_058	24,1		18,6		
MD_001_059	23,9	19,1	15,2	13,6	
MD_001_060	18,3	28,8	27	18,1	
MD_001_061	18,6	25,5	16,3		
MD_001_062	18,2	16,2	15,4		
MD_001_063	19,6	26,6			
MD_001_064	15,8	17,5	17		
MD_001_065	12,4	25	24,1		
MD_001_066	23,5	21,4	22,9		
MD_001_067	13,4				
MD_001_068	18,5		23,5		
MD_001_069	11,1				
MD_001_070	22,7				
MD_001_071	16,2				
MD_001_072	24,1				
MD_001_073	19				
MD_001_074	20,2	16,6			
MD_001_075	26,2	34,5			
MD_001_076	14,9	17,4			
MD_001_077	18,4	19,3			
MD_001_078	19,3				
MD_001_080	32,1	16,1			
MD_001_081	17,7	19,3			
MD_001_082	16,9	18,1			
MD_001_083	14,7	27,7			
MD_001_084	16,1	27,2			
MD_001_085	18,1	21,6			
MD_001_086	18,5				
MD_001_087	18,7				
MD_001_088	15				
MD_001_089	22,2				
MD_001_090	15,9	18,5			
MD_001_092	19,7				
MD_001_093	30,4	33,8			
MD_001_094	19				
MD_001_095	17,9				
MD_001_096	24,8				
MD_001_098	17				
MD_001_100	25,7				
MD_002_001	21				
MD_005_001	29,3	19,3			
MD_005_002					
MD_005_003	19,8				
MD_005_004	17,8				
MD_006_002	20,8	22,3	20	15,4	16,4
MD_006_003	19,5				
MD_006_004	17,3	19,8	22,7	25,1	16,9
MD_006_005	16	16,6	19,9	19,5	15,7
MD_006_006	18,1	20,7	20,8	21,5	20,5
MD_006_007	12,8				
MD_006_008	16,2	19,3			15,2
MD_006_009	14,5	15,8			
MD_006_010	22,5				35,9
MD_006_011	19,2				
MD_007_001	19,5	14,8			
MD_007_003	15,1				
MD_008_001					
MD_009_001	16,2	15,7		15,1	14,8
MD_009_002	24,7	21,6		19,4	
MD_009_003	18,5		16,7		
MD_009_004	16,3				
MD_009_005	19,4	13,2		15	13,8
MD_009_006	27,1		25,6		
MD_009_007	16,3	15,9		15,2	16,1
MD_009_008	16,6	17,1		16,9	18,6
MD_009_009	20	20,7		19,7	19,5
MD_009_010	17,8	19,2		18,4	18,7
MD_009_011	25,4	17,9			
MD_009_012	12,5		14,4		
MD_009_013	22,4	25,3		27,3	20,2
MD_009_014	13,6	14,7			29,5
MD_009_015	16,9			18,1	
MD_009_016	14,2	15,5			
MD_009_017	24,2	16,8			
MD_009_018	18,2	16,4		18,8	15,5
MD_009_019	15,1				
MD_009_020	16,5	15,4		16	16,1
MD_009_021	21,8				
MD_009_022	31		21	23,3	17,7
MD_009_023	24,2		17,3		
MD_009_024	15,5	16,1	13		16,9
MD_009_025	17,1		13,9	17	16,3
MD_009_026	15,8				
MD_009_027	16,1	17,5	18,9		14,9
MD_009_028	20,2				
MD_009_029	18		17,1		
MD_009_030	15,5	15,5			
MD_009_031	15,8	17,5		19,1	16,1
MD_009_032	25,4	18,5		20,9	20,4
MD_009_033	17,8	27,4			
MD_009_034	17				
MD_009_035	16,4	16,8			
MD_009_036	12,6	12,5			
MD_009_037	16,5				
MD_009_038	23,7		25		
MD_009_039	17	18		16,8	
MD_009_040	29	34,4		29	
MD_009_041	16,9	14,2	14,9		
MD_009_042	49,3	18,9	20,1		
MD_009_043	27,3				
MD_009_044	14,9				
MD_009_045	17,4	16,4	17,6		
MD_009_046	19,1	21,5	19,6		
MD_009_047	20,4		20,5		
MD_009_048	21,2		24,9		
MD_009_049	29,6	25,5			25,6
MD_009_050	18,2		17,7		
MD_009_051	19,1	17,1	17,1		
MD_009_052	15,8				
MD_009_053	16,9				
MD_009_054	13		12,5		
MD_009_055	15,1	18,1	17,1		17,8
MD_009_056	17,6	16,3			119,6
MD_009_057	23,6				
MD_009_058	22,6				
MD_009_059	36,4	22,5			18,6
MD_009_060	150,4				
MD_009_061	18,8				
MD_009_062					
MD_009_063	21				
MD_009_064	17,3				
MD_009_065	17,7				
Average	20,64	20,57	19,69	19,86	21,07

27. ECG

ECG procedure at screening (Day 1), at V3 (6 month) and V5 (12 month) to follow up the QT intervals for the enrolled subjects in the study. The ECGs was done locally at each study site, the results were analysed/interpreted by the local cardiologists. We did not expect any changes in QT intervals based on earlier research.[8]

Normal range of the QT interval ranges from 360 to 460 ms for adult women.
However, 10%-20% of otherwise healthy persons may have QTc values outside this range.
Of the baseline measurements, 12 women had a QTc value of less than 360.
At visit 3, 4 women had a QTc value of less than 360
At visit 4, 1 woman had a QTc value of less than 360
At visit 5, 3 women, had a QTc value of less than 360

None of the women had a QTc value of more than 460. These values have no clinical significance.

ECG QT interval in ms				
Visit nr	Baseline	Visit 3	Visit 4	Visit 5
N	112	52	21	58
Average	402,1	405,1	407,6	407

ECG QT interval in ms

Visit nr	Test results - Baseline	Test results - Visit 3	Test results - Visit 4	Test results - Visit 5
MD_001,001	370	370		334
MD_001,002	444		404	374
MD_001,003	405	335		374
MD_001,004	356	432		465
MD_001,005	450	428		463
MD_001,006	362	362		364
MD_001,007	384	340		421
MD_001,008				
MD_001,009	362	380		372
MD_001,010	427	425		448
MD_001,011	411			
MD_001,012	344	389		390
MD_001,013	366	378		
MD_001,014				
MD_001,015	431		356	344
MD_001,016	431	368		382
MD_001,017	368		404	401
MD_001,018	417	446		374
MD_001,019	403	421		407
MD_001,020	404	422		414
MD_001,021				
MD_001,022				
MD_001,023	354	412		369
MD_001,024	354	369		455
MD_001,025	406	424		394
MD_001,026	400	452		418
MD_001,027	359	448	431	390
MD_001,028	387	374		428
MD_001,029	436	396		414
MD_001,030	348	426		455
MD_001,031				
MD_001,032	404		408	388
MD_001,033	448	455		375
MD_001,034				
MD_001,035	396		410	371
MD_001,037		396	394	403
MD_001,038	429	414	390	392
MD_001,039	448		419	404
MD_001,040	416	343		390
MD_001,041		384		448
MD_001,042	448	397		413
MD_001,043	418	466		409
MD_001,044	440	453		407
MD_001,045	348	376		
MD_001,046	409	372		398
MD_001,047	396			
MD_001,048	347		367	
MD_001,049				
MD_001,050	404		393	397
MD_001,051	408	364		
MD_001,052	389	434		
MD_001,053	366		447	
MD_001,054		333		
MD_001,055	384	401		
MD_001,056	427	404	395	
MD_001,057	318	400		
MD_001,058	371	393		
MD_001,059	398			
MD_001,060				
MD_001,061	384			
MD_001,062				
MD_001,063	384			
MD_001,064	330	442		
MD_001,065	404	391		
MD_001,066		462		
MD_001,067				
MD_001,068	356	448		
MD_001,069	383			
MD_001,070				
MD_001,071				
MD_001,072	400			
MD_001,073				
MD_001,074	386			
MD_001,075	364			
MD_001,076	394			
MD_001,077	360			
MD_001,078				
MD_001,080	386			
MD_001,081	358			
MD_001,082	370			
MD_001,083	364			
MD_001,084	388			
MD_001,085	433			
MD_001,086	404			
MD_001,087	417			
MD_001,088				
MD_001,089				
MD_001,090	392			
MD_001,092	416			
MD_001,093	424			
MD_001,094	411			
MD_001,095	413			
MD_001,096				
MD_001,098	459			
MD_001,100	406			
MD_002,001				
MD_005,001				
MD_005,002				
MD_005,003	409			
MD_005,004	425			
MD_006,002		422	411	422
MD_006,003				
MD_006,004		428	419	413
MD_006,005		432	422	419
MD_006,006		426	435	424
MD_006,007				
MD_006,008	434			401
MD_006,009	404			
MD_006,010	419			421
MD_006,011	433			
MD_007,001				
MD_007,003	408			
MD_008,001				
MD_009,001				
MD_009,002	409			
MD_009,003	431			
MD_009,004	421			
MD_009,005	424			416
MD_009,006	445			
MD_009,007				432
MD_009,008	423			
MD_009,009				429
MD_009,010	419			
MD_009,011				
MD_009,012	434			
MD_009,013	411			403
MD_009,014	403			409
MD_009,015	406			
MD_009,016				
MD_009,017				
MD_009,018				438
MD_009,019				
MD_009,020	391			395
MD_009,021	425			
MD_009,022	380			415
MD_009,023	414			
MD_009,024	445			444
MD_009,025			402	420
MD_009,026				
MD_009,027	436			436
MD_009,028	386			
MD_009,029				
MD_009,030	396			
MD_009,031	403		428	406
MD_009,032			417	
MD_009,033				
MD_009,034				
MD_009,035	443			
MD_009,036				
MD_009,037				
MD_009,038				
MD_009,039				
MD_009,040				
MD_009,041		432		
MD_009,042				
MD_009,043				
MD_009,044	411			
MD_009,045				
MD_009,046	446			
MD_009,047		423		
MD_009,048		435		
MD_009,049	399			
MD_009,050				
MD_009,051		337		
MD_009,052				
MD_009,053				
MD_009,054				
MD_009,055				
MD_009,056	401			388
MD_009,057	429			
MD_009,058	443			
MD_009,059	415			392
MD_009,060				
MD_009,061				
MD_009,062	422			
MD_009,063	417			
MD_009,064				
MD_009,065				438
Average	**402,1**	**405,1**	**407,6**	**407,0**

28. ENDOMETRIUM

During every follow-up visit a vaginal ultrasound was performed by a physician who reported on endometrial thickness. When the ultrasound shows endometrial irregularities, an irregular cystic appearance, or an endometrial thickness >15 mm, a biopsy was taken to exclude a malignancy. If the biopsy showed PAEC, the study participant was kept in the study.

The average endometrial thickness did not change after using mifepristone for a year.

After 3 months appr 7 (7%) of 101 participants had an endometrial thickness>15 mm.
Of 4 participants the endometrium had normalized with the follow up visit after 6 months, 1 (< 1%) of the participants still had an endometrial thickness of more than 15 mm after 6 and 9 months but the endometrium had normalized with the follow up visit at 12 months. Of 2 participants there are no further data .

Of the 3 participants who developed an endometrial thickness after 6 and/or 9 months, the endometrium normalized with the next visits in 2 participants. Of 1 participant there is no follow up ultrasound available.

In total 10 of the 101 10%) participants developed an endometrial thickness at some point during the study, of these 9 had endometrium <15 mm with the final follow up visit. Of one participant the final follow up visit still has to take place. Pathology showed that these were all cases of PAEC.

Endometrial thickness					
Visit nr	1	2	3	4	5
N	178	101	76	63	60
>15 mm	0	7	3	3	0
%		6,9	3,9	4,8	0
Average	7,7	9,2	8,7	9,2	7,7

All participants who had an endometrium of > 15 mm, had a biopsy. All biopsies where reviewed by Porfessor Allistar, an expert on PAEC and he diagnosed all the changes PAEC, which is a as the benign and reversible change to the endometrium.

Actions:

1- The requirement for mandatory biopsies at 3, 6 and 12 months has been removed from the protocol. A biopsy is only performed if the endometrium is more than 15 mm.

2- Dr Allistor provided a training for the local pathologists so that they can analyse the endometrium following the WHO guidelines as put together by Prof Allistar.

Notes and Definitions

1. Physiological appearances are those described in the normal menstrual cycle (see Blaustein's Pathology of the Female Genital Tract).

2. Non-physiological appearances include any appearances that are not seen in the normal menstrual cycle, and will mainly include drug effect, but possibly other appearances such as endometrial polyp. The appearances which it is expected may be associated with PRM drug effect include:
   (i) Endometrial gland dilatation – a variable proportion of glands may show cystic dilatation.

(ii) Gland architecture – non-dilated glands may show tortuosity of architecture similar to that seen in the normal mid-secretory phase, but with only abortive or partially developed indicators of secretory activity (cytoplasmic vacuolation, apical secretory blebbing), and there may be mitoses in glandular epithelial cells.

(iii) Glands will usually be lined by a single layer of non-stratified epithelial cells of cuboidal or columnar type. (This contrasts with the stratified appearance usually seen in endometrial hyperplasia). Epithelial cells may show ciliated or eosinophilic metaplasia.

(iv) Stroma may be compact and cellular, or with alternating areas of looser more oedematous appearances. Mitotic activity may be present, but is expected to be infrequent.

(v) Vessels - ectatic capillary channels may be present, or "chicken wire" capillaries. Thick walled muscular arterioles may be present.

3. Gland dilatation is usually easily recognizable, but can be defined as a gland showing an open lumen that forms a space greater than 10 times the epithelial thickness.

4. Non-dilated gland architecture may be assessed as to whether there are distorted and crowded forms present, as seen in the so-called "disordered proliferative pattern" (see Blaustein's Pathology of the Female Genital Tract). Architectural abnormalities fall short of that seen in complex endometrial hyperplasia.

5. Gland epithelium may be classified as "inactive" or "proliferative". This will be based on assessment of the following 3 features:
   (i) Epithelial stratification – a single layer of cells indicates an inactive epithelium. (Tangential sectioning may give a false appearance of stratification).
   (ii) Cell height – cuboidal cells indicate inactive epithelium. Ciliated or eosinophilic metaplasia is frequently associated with inactive appearances. Tall columnar cells are usually associated with proliferative epithelium; they usually show nuclear stratification.
   (iii) Mitotic activity in glands is associated with proliferative appearances, but note that occasional mitoses may be seen in the inactive epithelium associated with the drug effect. Therefore, epithelium may be classified as "inactive" even in the presence of a small number of mitoses. Frequent mitoses are a marker of proliferative epithelium.

6. Endometrial hyperplasia: if the appearances are considered to represent hyperplasia of endometrium, please classify according to **both** WHO definitions (1994 and 2014) (see Blaustein for definitions and images).

7. If necessary, there is an opportunity to provide additional comments or descriptions in the free text area at the end of the form.

Endometrium					
Visit nr	1	2	3	4	5
MD_001,001	3,3	7,3	7,5	7	3
MD_001,002	14	12	4,2	6,4	5
MD_001,003	7	10	12	9	15
MD_001,004	9,1	6,1	5,5	6	11
MD_001,005	8	8	11	7,4	4,2
MD_001,006	5	17	6,4	25,5	10
MD_001,007	8	8	12	10	7,1
MD_001,008	10				
MD_001,009	4,1	5	6	5,1	6,7
MD_001,010	8	7	9	9	5
MD_001,011	5				
MD_001,012	10	6,3	11	10	7,7
MD_001,013	5,6	9	7		
MD_001,014					
MD_001,015	12	6,7	10	8,5	8
MD_001,016	11	14	7,3	13	7,3
MD_001,017	6,6	7	15	4	5
MD_001,018	9	8	11	11	10
MD_001,019	3	11	8,5	7	7
MD_001,020	11	8	6,7	11	7,7
MD_001,021	12	5,7			
MD_001,022					
MD_001,023	14	16	15	10	12
MD_001,024	4	12	13	9	13
MD_001,025	6,5	16	23	26	12
MD_001,026	10	5	7	6,4	4,2
MD_001,027	4	9	11	9,2	10
MD_001,028	10	7	12	7	14
MD_001,029	4	7	8	6	7
MD_001,030	12	15	8,5	9	6
MD_001,031	4				
MD_001,032	8	10	12	27	4,6
MD_001,033	8		5	9	13
MD_001,034	9				
MD_001,035	12,1	9,6	13	10	9
MD_001,037	7	10	13	12	10
MD_001,038	7	11	13	7	7
MD_001,039	9,5	5	10	8	8,9
MD_001,040	7,4	10	6,2		9
MD_001,041	10	16,5	5	9	6
MD_001,042	10	4	4,5	7,7	8
MD_001,043	8		8	7	6
MD_001,044	11	9	11	7	5
MD_001,045	6,6	5	6,3		
MD_001,046	10	9	5	8	8
MD_001,047	12,7	6,8	8	3,18	
MD_001,048	7	12		9	
MD_001,049	3,5	8	9		
MD_001,050	8,5	9		5	4,1
MD_001,051	8,5	8	7		
MD_001,052	5,3	10	7		
MD_001,053	5	9	10	10	
MD_001,054	3,7	6	7		
MD_001,055	6,4		7		
MD_001,056	7	10	12	11	
MD_001,057	10		5,6		
MD_001,058	8		12		
MD_001,059	14	12	5,9	5	
MD_001,060	5	10	6		
MD_001,061	9,5	8,4			
MD_001,062	5,5	8,5			
MD_001,063	8,7	9			
MD_001,064	11	9	10		
MD_001,065	11,6	8	6,6		
MD_001,066	7,5	5,3	4,5		
MD_001,067	10				
MD_001,068	2,6				
MD_001,069	10				
MD_001,070					
MD_001,071	2,4				
MD_001,072	10				
MD_001,073					
MD_001,074	10	10			
MD_001,075	8,5				
MD_001,076	4,5	11			
MD_001,077	6	7			
MD_001,078	5,4				
MD_001,080	8,2	11			
MD_001,081	8	10			
MD_001,082	12				
MD_001,083	8,7	15,9			
MD_001,084	7				
MD_001,085	10				
MD_001,086	5,8				
MD_001,087	4				
MD_001,088					
MD_001,089					
MD_001,090	9,7	17,9			
MD_001,092	4,5				
MD_001,093	3	3			
MD_001,094	8				
MD_001,095	8				
MD_001,096					
MD_001,098	11				
MD_001,100	8,3				
MD_002,001	8				
MD_005,001	5,1	13			
MD_005,002					
MD_005,003	3,9		26	26	
MD_005,004	9				
MD_006,002	8	13	10	6,8	6
MD_006,003	12				
MD_006,004	7	5	10	8,6	5,5
MD_006,005	8		6	4,8	3,5
MD_006,006	6	6,3	5,5	7	5,5
MD_006,007	5,6				
MD_006,008	8,5	8			6
MD_006,009	11				
MD_006,010	4,5				6,9
MD_006,011	3				
MD_007,001	7	6,6			
MD_007,003	2,8				
MD_008,001					
MD_009,001	5	5		7	8,5
MD_009,002	4,5	4		12	
MD_009,003	12,5		9,4		
MD_009,004	10				
MD_009,005	8	14,1		13	-99
MD_009,006	8		8		
MD_009,007	8	-99		11	5,9
MD_009,008	9	7		5,1	
MD_009,009	9	9,6		12	3,4
MD_009,010	12	12		15	
MD_009,011	9	3,4			
MD_009,012	9		7		
MD_009,013	6	4		5,7	5,8
MD_009,014	8	18		8,6	15
MD_009,015	6			6,5	
MD_009,016	9,7	8			
MD_009,017	10	12			
MD_009,018	6	8,3		4,5	8
MD_009,019	9				
MD_009,020	8	10		11	9,1
MD_009,021	3				
MD_009,022	9		3	7,2	0,8
MD_009,023	16	10	13		
MD_009,024	9	9,5	5,3		10
MD_009,025	10		18	7	10,3
MD_009,026	8				
MD_009,027	12	10	11		11
MD_009,028	7				
MD_009,029	5		3		
MD_009,030	5	4			
MD_009,031	4	3,7		5,2	8,9
MD_009,032	8,9	12		6,7	1
MD_009,033		11			
MD_009,034	2				
MD_009,035	7	5			
MD_009,036	7	10			
MD_009,037	13				
MD_009,038	9		13		
MD_009,039	4	9,3			
MD_009,040	7	11		0,6	
MD_009,041	5	9	4		
MD_009,042	11	7,6	1		
MD_009,043	7,5				
MD_009,044	5,6		0,5		
MD_009,045	9,7	15			
MD_009,046	8,2	10			
MD_009,047	3,5		4		
MD_009,048	11				
MD_009,049	4	15			
MD_009,050	12				
MD_009,051	3,4		4,8		
MD_009,052	7,3				
MD_009,053	10				
MD_009,054	4		3		
MD_009,055	10	8,3	7,6		7
MD_009,056	3,9	5	14		8,4
MD_009,057	12				
MD_009,058	10	9			
MD_009,059	11	11			14
MD_009,060	2,9				
MD_009,061	12				
MD_009,062	8,2				
MD_009,063	5,3				
MD_009,064	0,7				
MD_009,065	0,9				5
Average	7,73	8,14	8,74	9,17	5,69

29. SERIOUS ADVERSE EVENTS

There were 5 reported SAE's. Three were pregnancies as earlier described.

One SAE was registered on 27 Nov2023. Participant **MD-006.003** experienced menorrhagia, posthemorrhagic anaemia of moderate severity before start of study medication and had no relation to the study medication. The SAE was resolved. She was further excluded from the study on her own request.

Another reported AE's concerned one participant who experienced side effects of nausea, hotflushes and headache.

Participant Id	event	action
MD_005.002	pregnancy	termination of pregnancy
MD_001.017	experenced nausea, horflushes and headache	no
MD_006.009	pregnancy	termination of pregnancy
MD_006.003	before start of the medication experenced metthorragia	did not start with study medication and withdrew conc
MD_001.067	ectopic pregnancy	laporioscopic removal ectopic pregnancy

30. BLEEDING PATTERN

Of the 147 participants who provided some data through the daily diary app 26 (17%) (reported 0 days of bleeding or spotting. Reported less than … days of bleeding or spotting per

Days bleeding																									
	2023					2024												2025							total days of t
Row Labels	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	
MD_001.015				0	0	0	0	0	0	0	0	0	0	0	0										
MD_001.023			0	0	0	0	0	0	0	0	0	0													0
MD_001.029				0	0	0	0	0	0	0	0	0	0	0	0	0	0	0							0
MD_001.033								0				0	0	0	0	0	0	0	0						0
MD_001.037							0	0	0	0	0	0	0	0	0	0	0	0	0	0					0
MD_001.040								0	0	0	0	0	0	0	0	0	0	0	0	0					0
MD_001.043									0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MD_001.044									0	0	0	0	0	0											0
MD_001.047											0	0	0	0	0	0	0	0	0	0	0				0
MD_001.049												0	0	0	0	0	0	0	0	0	0	0	0		0
MD_001.051															0	0	0	0	0	0	0	0			0
MD_001.053													0	0	0	0	0	0	0	0	0				0
MD_001.065																0	0	0	0	0	0	0	0		0
MD_001.069																					0				0
MD_001.076																		0	0	0	0	0	0		0
MD_001.078																		0							0
MD_001.082																		0	0		0	0	0		0
MD_001.086																							0		0
MD_001.087																						0	0		0
MD_001.089																							0		0
MD_005.002									0	0															0
MD_007.001				0	0	0	0	0	0																0
md_009.005				0	0	0	0	0	0	0	0	0	0	0	0	0									0
MD_009.006				0	0	0	0	0	0																0
MD_009.025								0																	0
MD_009.027								0							0										0
MD_001.013		0	0	0	0	1	0	0																	1
MD_001.021			0	1	0	0	0	0	0																1
MD_001.041							1	0	0	0	0	0	0	0	0			0	0						1
MD_001.068																0	0	1	0						1
MD_006.010																							1	0	1
MD_009.012							0	1	0					0											1
MD_009.016					0	0	0	1																	1
MD_009.019						1	0	0																	1
MD_009.022						0	1	0																	1
MD_009.026								0	1																1
MD_001.063																0	1	0	1						2
MD_001.067																0	0	0	2						2
MD_001.085																					2	0			2
MD_009.021								0	0	2															2
MD_001.016	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0									3
MD_001.045									1	0	0	0	0	2	0	0	0	0	0	0					3
MD_001.054															3	0	0	0	0	0	0	0	0		3
MD_005.004											1	1	0	0	1										3
MD_009.049															1	1	0	1	0	0					3
MD_009.058																1	1	0	1	0					3
MD_001.001		1	1	0	0	0	0	0	0	0	1	0	0	0	1										4
MD_001.039							0	0	0	0	0	0	0	0	0	0	0	0	2	2					4
MD_001.046								0	0	1	2	0	0	0								1			4
MD_001.080																		0	0	1	0	1	1	1	4
MD_001.092																						4			4
MD_009.059																		1	0	1	1	0	1		4
MD_001.007		0	0	4	0	0	0	0	0	0	0	0	0	1	0										5
MD_001.018							0	0	0	0	0	0	3	2	0										5
MD_001.073																					1	2	2	0	5
MD_001.093																					1	1	1	2	5
MD_009.039											0	5													5
MD_009.044														5	0										5
MD_009.048														1	0	0	1	1	1	0	1				5
MD_009.056																3	0	1	1	0					5
MD_001.003		1	1	3	1	0	0	0	0	0	0	0	0	0	0	0									6
MD_001.010			3	3	0	0	0	0	0	0	0	0	0	0	0	0									6
MD_001.052														5	1	0	0	0	0	0	0	0	0		6
MD_001.061															2	0	1	1	1	0	0	0	0	0	6
MD_009.014					0	0	0	0	0	0	1	1	1	1	1	0	0	1							6
MD_009.037											0	6													6
MD_009.047															6										6
MD_009.051															2	0	1	1	0	1	1				6
MD_009.052															1	1	3	1	0	0					6
MD_009.057																3	1	1	1	0					6
MD_001.057															6	1	0	0	0	0	0	0	0		7
MD_009.045														7	0										7
MD_009.046														4	3										7
MD_001.024			4	4	0	0	0	0	0	0	0	0	0	0	0	0									8
MD_001.030					4	0	0	0	2	0	1	0	1	0	0	0	0								8
MD_001.035							2	1	0	1	0	0	2	0	1	0	1	0	0						8
MD_001.064																0	2	1	1	1	0	0	3		8
MD_009.023							0	3	4	1															8
MD_009.035									0	3	5														8
MD_009.038										0	5	1	0	1	1	0									8
MD_009.040											0	1	1	0	1	1	0	1	1	1	0	1			8
MD_009.053															3	3	1	1	0						8
MD_001.020			3	3	3	0	0	0	0	0	0	0	0	0	0	0									9
MD_009.007			0	0	0	0	0	0	0	3	3	2	0	0	1	0									9
MD_001.048												1	4	3	0	2									10
MD_001.066																2	1	2	3			2			10
MD_009.002			0	0	0	0	0	0	2	0	4	4	0												10
MD_009.015					0	0	0	0	0	3	4	3													10
MD_009.041														6	0	1	1	1	0	1					10
MD_001.055														1	1	2	2	1	0	3	0	1			11
MD_009.030								0	3	5	4	0													12
MD_009.054														2	3	4	0	1	1	1	0				12
MD_009.003			0	0	0	0	0	0	0	3	5	1	4												13
MD_001.004			0		0	0	2	6	4	2	0	0	0	0	0										14
MD_009.024							0	2	4	0	4	1	0	1	0	1	0	1	0						14
MD_009.033								0	3	6	5														14
MD_009.042														7	4	1	0	0	1	0	1				14
MD_001.042								7	5	0	0	0	0	0	0	0	0	0	1	2	0				15
MD_001.060														5	8	2	0	0	0	0	0	0	0		15
MD_001.062																4	2	2	0	4	3				15
MD_009.031									0	0	4	4	1	1	1	1	1	1	0	0					15
MD_001.058			4	4	0	0	0	0	0	0	0	0	0	0	0	1	1	2	2	1	0	0	1	0	0
MD_006.004					0	0	0	0	0	2		0	0	5	0	0	5	5							17
MD_006.008																			6	1		5	5	0	17
MD_007.003															0	5	6	2	1	0	1	1	1		17
MD_009.008				0	0	0	0	0	3	4	4	4	0	1	1	0									17
MD_009.029								5	4	5	3	0													17
MD_001.075																		1	3	5	4	5	0		18
MD_001.077																		5	4	5	4	0	0		18
MD_001.084																				10	8	0			18
MD_005.003											5	0	0	0	0	0	0	4	1	0	3	2	3		18
MD_009.011					0	0	0	0	3	5	1	9	0												18
MD_009.032									4	4	6	1	0	0	1	1	0	0	1	0					18
MD_001.017			0	3	0	0	0	13	3	0	0	0	0	0											19
MD_009.009				0	0	0	0	0	5	5	4	2	2	1	0	0									19
MD_009.036										0	7	6	6	0											19
MD_001.083																		1	1	2	4	5	7		20
MD_009.020							0	0	0	3	3	4	3	5	0	1	0	1							20
MD_001.059														0	0	2	0	6	7	6		0			21
MD_009.050												4	3	5	6	0	0	1	1	1	0	0			21
MD_009.017							1	2	1	4	5	4	5												22
MD_001.038								2	1	0	8	0	3	0	3	3	2	1	0	0					23
MD_001.002		4	5	9	4	3	0	0	0	0	0	0	0	0	0										25
MD_001.019			0	4	0	4	4	4	0	2	3	2	0	0	2										25
MD_001.074																			0	4	6	6	5	4	25
MD_009.013					0	0	1	0	2	5	5	3	7	1	0	0	1								25
MD_009.018						0	0	0	4	2	2	5	6	1	5	0	1								26
MD_001.050											3	6	7	0	4	1	1	2	0	0	1	1	1		27
MD_001.081																		5	5	4	7	2	5		28
MD_001.026			1	2	3	3	6	4	3	3	4	0	0	0	0										29
MD_006.009																		3	8	11	7	0			29
MD_009.010				0	0	1	3	0	5	4	0	8	5	1	2	0									29
MD_001.028			1	3	0	0	3	1	0	0	0	4	0	2	0	0	4	2	10						30
MD_001.090																					4	0	17	10	31
MD_001.056														3	4	4	5	4	4	5	5				34
MD_009.001			0	4	5	6	2	6	4	6	4	0	0	3											40
MD_001.012				1	5	1	2	4	6	4	3	4	8	4	3	2									47
MD_001.032						2	7	5	5	4	2	3	4	4	3	3	3	3							48
MD_006.005					6	4	5	8	6	4	3	6	5	0	5	0	0								52
MD_006.006									4	5	4	3	4	5	2	6	5	4	3	6	4				55
MD_001.005		6	6	3	0	4	11	5	5	5	0	5	2	4											56
MD_005.001							0	3	1	5	5	5	9	2	6	5	4	6	5						56
MD_001.006			4	0	0	18	2	0	15	6	6	4	4	0	0										59
MD_001.027				1	3	5	8	6	8	6	0	6	6	4	5	2									60
Md_006.002					4	14	10	7	0	7	5	1	2	20	4	4	0								78
MD_001.025			4	0	0	1	1	0	2	11	7	15	27	18	19										105
MD_001.009			2	2	7	11	16	7	12	4	5	7	12	13	6	3									107

31. COMPLAINTS

Of the 147 participants who filled in the dairy app, 96 (65%) reported no complaints at all.

Of the 51 (35%) who reported one or more complaints:

- 25 (in total 17%) reported pain-full breasts at least once.
- 22 (14%) reported mood-changes at least once
- 14 (9%) reported hot flushed once at least once
- 28 (19%) reported nausea at least once
- 34 (23%) reported headache at least once
- 8 (5%) reported dry eyes at least once

Complaints	Sum of other	Sum of painfull breats	Sum of mood changes	Sum of nausea	Sum of hot fluches	Sum of headache	Sum of dry eye
MD_006.004	12	9	2	0	11	36	1
MD_001.090	3	0	4	0	3	4	0
MD_001.045	0	0	0	0	1	0	0
MD_001.060	0	12	14	0	0	0	0
MD_006.010	2	1	2	0	0	0	0
MD_001.032	0	4	1	0	0	0	0
MD_009.018	0	2	0	0	0	0	0
MD_001.067	1	1	0	0	0	0	0
MD_001.001	0	0	0	0	0	0	0
MD_001.002	0	0	0	0	0	0	0
MD_001.005	0	0	0	0	0	0	0
MD_001.007	0	0	0	0	0	0	0
MD_001.015	0	0	0	0	0	0	0
MD_001.016	0	0	0	0	0	0	0
MD_001.019	0	0	0	0	0	0	0
MD_001.021	0	0	0	0	0	0	0
MD_001.023	0	0	0	0	0	0	0
MD_001.024	0	0	0	0	0	0	0
MD_001.027	0	0	0	0	0	0	0
MD_001.028	0	0	0	0	0	0	0
MD_001.029	0	0	0	0	0	0	0
MD_001.033	0	0	0	0	0	0	0
MD_001.035	0	0	0	0	0	0	0
MD_001.037	0	0	0	0	0	0	0
MD_001.039	0	0	0	0	0	0	0
MD_001.040	0	0	0	0	0	0	0
MD_001.041	0	0	0	0	0	0	0
MD_001.042	0	0	0	0	0	0	0
MD_001.043	0	0	0	0	0	0	0
MD_001.044	0	0	0	0	0	0	0
MD_001.046	0	0	0	0	0	0	0
MD_001.047	0	0	0	0	0	0	0
MD_001.049	0	0	0	0	0	0	0
MD_001.051	0	0	0	0	0	0	0
MD_001.052	0	0	0	0	0	0	0
MD_001.053	0	0	0	0	0	0	0
MD_001.055	0	0	0	0	0	0	0
MD_001.056	0	0	0	0	0	0	0
MD_001.057	0	0	0	0	0	0	0
MD_001.058	0	0	0	0	0	0	0
MD_001.059	0	0	0	0	0	0	0
MD_001.063	0	0	0	0	0	0	0
MD_001.065	0	0	0	0	0	0	0
MD_001.066	0	0	0	0	0	0	0
MD_001.069	0	0	0	0	0	0	0
MD_001.073	0	0	0	0	0	0	0
MD_001.074	0	0	0	0	0	0	0
MD_001.075	0	0	0	0	0	0	0
MD_001.076	0	0	0	0	0	0	0
MD_001.078	0	0	0	0	0	0	0
MD_001.080	0	0	0	0	0	0	0
MD_001.081	0	0	0	0	0	0	0
MD_001.082	0	0	0	0	0	0	0
MD_001.083	0	0	0	0	0	0	0
MD_001.085	0	0	0	0	0	0	0
MD_001.086	0	0	0	0	0	0	0
MD_001.087	0	0	0	0	0	0	0
MD_001.089	0	0	0	0	0	0	0
MD_001.092	0	0	0	0	0	0	0
MD_001.093	0	0	0	0	0	0	0
MD_005.002	0	0	0	0	0	0	0
MD_005.003	0	0	0	0	0	0	0
MD_006.008	0	0	0	0	0	0	0
MD_007.001	0	0	0	0	0	0	0
MD_007.003	0	0	0	0	0	0	0
MD_009.001	0	0	0	0	0	0	0
MD_009.002	0	0	0	0	0	0	0
md_009.005	0	0	0	0	0	0	0
MD_009.007	0	0	0	0	0	0	0
MD_009.009	0	0	0	0	0	0	0
MD_009.010	0	0	0	0	0	0	0
MD_009.011	0	0	0	0	0	0	0
MD_009.012	0	0	0	0	0	0	0
MD_009.013	0	0	0	0	0	0	0
MD_009.014	0	0	0	0	0	0	0
MD_009.015	0	0	0	0	0	0	0
MD_009.016	0	0	0	0	0	0	0
MD_009.017	0	0	0	0	0	0	0
MD_009.020	0	0	0	0	0	0	0
MD_009.025	0	0	0	0	0	0	0
MD_009.026	0	0	0	0	0	0	0
MD_009.029	0	0	0	0	0	0	0
MD_009.030	0	0	0	0	0	0	0
MD_009.031	0	0	0	0	0	0	0
MD_009.033	0	0	0	0	0	0	0
MD_009.035	0	0	0	0	0	0	0
MD_009.037	0	0	0	0	0	0	0
MD_009.040	0	0	0	0	0	0	0
MD_009.041	0	0	0	0	0	0	0
MD_009.044	0	0	0	0	0	0	0
MD_009.045	0	0	0	0	0	0	0
MD_009.046	0	0	0	0	0	0	0
MD_009.047	0	0	0	0	0	0	0
MD_009.048	0	0	0	0	0	0	0
MD_009.049	0	0	0	0	0	0	0
MD_009.050	0	0	0	0	0	0	0
MD_009.051	0	0	0	0	0	0	0
MD_009.052	0	0	0	0	0	0	0
MD_009.053	0	0	0	0	0	0	0
MD_009.054	0	0	0	0	0	0	0
MD_009.057	0	0	0	0	0	0	0
MD_009.058	0	0	0	0	0	0	0
MD_009.059	0	0	0	0	0	0	0
MD_001.077	1	0	0	0	0	0	0
MD_001.061	2	0	0	0	0	0	0
MD_001.084	0	0	1	0	0	1	0
MD_009.024	0	2	0	0	0	1	0
MD_001.004	0	1	0	0	0	1	0
MD_001.010	0	1	0	0	0	1	0
MD_001.003	0	0	0	0	0	1	0
MD_001.020	0	0	0	0	0	1	0
MD_009.003	0	0	0	0	0	1	0
MD_009.038	0	0	0	0	0	1	0
MD_005.001	0	0	0	0	0	2	0
MD_009.021	0	0	0	0	0	2	0
MD_009.039	0	0	0	0	0	2	0
MD_001.064	1	3	3	0	0	3	2
MD_001.026	8	12	10	0	0	3	0
MD_001.048	0	0	12	0	0	11	1
MD_001.018	2	3	3	1	67	3	0
Md_006.002	1	0	0	1	17	11	0
MD_005.004	0	1	1	1	1	1	0
MD_001.025	2	1	0	1	0	0	0
MD_009.022	0	0	0	1	0	0	0
MD_009.042	0	0	0	1	0	0	0
MD_009.056	0	0	0	1	0	0	0
MD_001.006	11	3	0	1	0	1	0
MD_009.006	0	0	0	1	0	1	0
MD_001.054	0	0	0	1	0	1	0
MD_006.009	4	5	4	1	0	16	0
MD_001.013	0	63	9	2	83	49	1
MD_006.005	8	1	2	2	2	1	0
MD_009.019	0	0	0	2	0	0	0
MD_009.023	0	0	0	2	0	0	0
MD_009.027	0	0	0	2	0	0	0
MD_009.032	0	0	0	2	0	0	0
MD_009.036	0	0	0	2	0	0	0
MD_009.008	0	0	0	2	0	2	0
MD_001.038	4	0	1	2	0	5	0
MD_001.068	2	1	13	2	0	8	0
MD_001.030	0	15	4	3	1	1	0
MD_001.062	4	0	0	3	0	0	0
MD_001.050	1	1	19	6	15	22	2
MD_001.017	6	5	8	8	11	9	8
MD_006.006	18	16	16	8	2	9	5
MD_001.012	5	15	2	17	1	23	2
MD_001.009	10	64	67	63	110	176	2

32. DISCUSSION AND OVERALL CONCLUSIONS

There is an unmet need for a contraceptive method that is easy to use, effective on demand, and free from estrogen-related side effects. Mifepristone, a well-studied progesterone receptor antagonist with a strong safety profile, was investigated for its potential as a once-weekly oral contraceptive.
Mifepristone 50 mg inhibits ovulation and reduces endometrial receptivity. Prior studies showed promising contraceptive efficacy at weekly doses of 25–50 mg, with no pregnancies reported in hundreds of cycles. The current study aimed to assess long-term efficacy, safety, and acceptability of 50 mg Mifepristone taken weekly.

This is the largest study so far that investigated the efficacy and safety of once a week mifepristone 50 mg as a weekly contraceptive.

The study was approved in Moldova in May 2022, with the aim to include 949 women (aged 18–35) that would use mifepristone 50 mg once week as a contraceptive for 12 months. Participants used an app to log medication use, intercourse, side effects, and pregnancy tests. Safety was monitored via liver tests, ultrasounds, ECGs, and biopsies when necessary.
Although recruitment began in August 2023, serious data integrity issues emerged at Site MD010 in 2025. A large-scale verification revealed widespread fraud: most participants at that site were not taking the study drug, and some were told to lie about their involvement. The site was closed, and all data from MD010 were excluded from analysis. Regulatory authorities ordered further audits and halted enrolment across all sites. Funding was withdrawn, and the study was formally closed in July 2025.
Data from 173 study participants after excluding the participants from site 10 were analysed. During the stuy there were 3 pregnancies in 1040 onprotected cycles. This meand that actual use Pearl Index so far is 3,46.
The only safety concern that needs further analyses was the temporary increased liver functions above 2- 3 UNL for bilirubin and more than 3 UNL for ALAT.

The method was very acceptable with only 35% of participants reported one or more complaints. Most women experienced amenorrhea

33. REFERENCE LIST

[i] https://www.medicines.org.uk/emc/product/3783/smpc
[2] C.Gerlinger at all, Recommendation for confidence interval and sample size calculation for the Pearl index, European Journal of contraception and reproductive health Care 2003; 8: 87-92

[4] Sun X, He L, Liu L, Wang S. Maternal age and progesterone levels at trigger day as independent predictors of clinical pregnancy in poor ovarian responders undergoing IVF/ICSI: a retrospective analysis. Front Endocrinol (Lausanne). 2025 Jun 23;16:1593298. doi: 10.3389/fendo.2025.1593298. PMID: 40626235; PMCID: PMC12229858.)
[5] see guidelines EMA ULIPRISTAL ACETATE 3 https://www.ema.europa.eu/en/documents/press-release/esmya-new-measures-minimise-risk-rare-serious-liver-injury_en.pdf
[6] https://www.fda.gov/media/116737/download
[7] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/drug-induced-liver-injury-premarketing-clinical-evaluation
[8] Borje Darpo etal, Assessment of the cardiac safety and pharmacokinetics of a short course, twice daily dose of orally-administered mifepristone in healthy male subjects, Cardiol J, 2013;20(2):152-60.
DOI: 10.5603/CJ.2013.0028