Clinical trial results:
Efficacy of Very Early Medical Abortion – a randomized controlled non-inferiority trial

Summary

EudraCT number	2018-003675-35
Trial protocol	SE FI AT DK
Global end of trial date	06 June 2023

Results information

Result version number	v1 (current)
This version publication date	27 February 2025
First version publication date	27 February 2025

Trial information

Trial identification

Sponsor protocol code	WV2018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Karolinska Institutet
Sponsor organisation address	Nobels väg 6, Solna, Sweden, 17177
Public contact	Kristina Gemzell Danielsson, Karolinska Instituet, 46 08517700002128, kristina.gemzell@ki.se
Scientific contact	Kristina Gemzell Danielsson, Karolinska Instituet, 46 08517700002128, kristina.gemzell@ki.se

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 June 2023
Global end of trial reached?	Yes
Global end of trial date	06 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate is if the efficacy of VEMA is non-inferior within a non-inferiority margin of 3 percent to delayed abortion treatment initiated when an intrauterine pregnancy (IUP) can be confirmed on ultrasound?

Protection of trial subjects:

The trial protocol was approved by the Swedish Ethical Review Authority and local ethics committee at each trial site or in each country. Participants were included after providing written informed consent. An external monitor and data and safety monitoring board were appointed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 668
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Denmark: 57
Country: Number of subjects enrolled	Finland: 92
Country: Number of subjects enrolled	Australia: 23
Country: Number of subjects enrolled	Norway: 24
Country: Number of subjects enrolled	New Zealand: 199
Country: Number of subjects enrolled	Nepal: 400
Country: Number of subjects enrolled	United Kingdom: 39
Worldwide total number of subjects	1504
EEA total number of subjects	843

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	1504
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial took place at 26 sites in nine countries from March 2019 through April 2023. Women seeking medication abortion with a maximum estimated gestational
length of 42 days and an unconfirmed intrauterine pregnancy on vaginal ultrasound examination were screened for inclusion.

Pre-assignment

Screening details:

Women were eligible if they were 18 years of age or older, spoke English or a local language, and provided informed consent. Exclusion criteria were symptoms or signs of pathologic pregnancy, risk factors for ectopic pregnancy or any contraindications to medication abortion.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Very Early Medical Abortion (VEMA)

Arm description:

Participants in the early-start group initiated medication abortion on the day of or the day after trial inclusion.

Arm type	Intervention, early treatment (VEMA)
Investigational medicinal product name	mifepristone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All the participants received the World Health Organization–recommended protocol for medication abortion: mifepristone at a dose of 200 mg orally, followed 24 to 48 hours later by misoprostol at a dose of 800 µg administered vaginally, sublingually, or buccally according to local standard practice. An additional dose of misoprostol (400 µg) was administered if bleeding
had not started within 3 hours (except in Australia). Oral analgesia was offered according to local clinical routine with a combination of nonsteroidal antiinflammatory drugs and paracetamol with repeat doses or oral opioids (or both) if needed.

Arm title	Standard

Arm description:

Treatment for participants in the standard group was delayed until a repeat ultrasound examination on trial day 7 (with a window of ±2 days) visualized an intrauterine pregnancy.

Arm type	Standard intervention
Investigational medicinal product name	mifepristone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

All the participants received the World Health Organization–recommended protocol for medication abortion: mifepristone at a dose of 200 mg orally, followed 24 to 48 hours later by misoprostol at a dose

of 800 µg administered vaginally, sublingually, or buccally according to local standard practice. An additional dose of misoprostol (400 µg) was administered if bleeding
had not started within 3 hours (except in Australia). Oral analgesia was offered according to local clinical routine with a combination of nonsteroidal antiinflammatory drugs and paracetamol with repeat doses or oral opioids (or both) if needed.

Number of subjects in period 1[1]	Very Early Medical Abortion (VEMA)	Standard
Started	741	724
Completed	693	574
Not completed	48	150
Pathological pregnancy	21	104
Lost to follow-up	19	27
Protocol deviation	8	19

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 1504 participants were initially enrolled - 754 assigned to Very early medication abortion (VEMA), however 13 were excluded prior to treatment - 750 were assigned to Standard medication abortion but 26 were excluded prior to treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Very Early Medical Abortion (VEMA)
Reporting group description:	
Participants in the early-start group initiated medication abortion on the day of or the day after trial inclusion.	

Reporting group title	Standard
Reporting group description:	
Treatment for participants in the standard group was delayed until a repeat ultrasound examination on trial day 7 (with a window of ±2 days) visualized an intrauterine pregnancy.	

Reporting group values	Very Early Medical Abortion (VEMA)	Standard	Total
Number of subjects	741	724	1465
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	29.6	29.7	
standard deviation	± 6.4	± 6.5	-
Gender categorical Units: Subjects			
Female	741	724	1465
Male	0	0	0

End points

End points reporting groups

Reporting group title	Very Early Medical Abortion (VEMA)

Reporting group description:

Participants in the early-start group initiated medication abortion on the day of or the day after trial inclusion.

Reporting group title	Standard

Reporting group description:

Treatment for participants in the standard group was delayed until a repeat ultrasound examination on trial day 7 (with a window of ±2 days) visualized an intrauterine pregnancy.

Primary: Complete abortion without ongoing pregnancy or surgical intervention

End point title	Complete abortion without ongoing pregnancy or surgical intervention

End point description:

End point type	Primary

End point timeframe:

Per protocol

End point values	Very Early Medical Abortion (VEMA)	Standard		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	710	688		
Units: Participants	676	656		

Statistical analyses

Statistical analysis title	Risk difference STANDARD-VEMA
Comparison groups	Very Early Medical Abortion (VEMA) v Standard
Number of subjects included in analysis	1398
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9
Method	Proportion test
Parameter estimate	Risk difference (RD)
Point estimate	-0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	2.1

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Per protocol	
Assessment type	Systematic

Dictionary used	
Dictionary name	NA
Dictionary version	NA

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 1465 (1.16%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Surgical and medical procedures			
Laparoscopy			
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 1465 (0.55%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 0		
Laparotomy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 1465 (0.07%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Uterine aspiration	Additional description: Uterine aspiration (in-patient)		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 1465 (0.20%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Medical treatment			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 1465 (0.07%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Bleeding	Additional description: Bleeding (vaginal/abdominal)		
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 1465 (0.34%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 1465 (0.20%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 1465 (2.73%)		
Investigations			
Additional shcg test			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 1465 (0.07%)		
occurrences (all)	1		
Surgical and medical procedures			
Treatment for ectopic pregnancy			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 1465 (0.20%)		
occurrences (all)	3		
Nervous system disorders			
Pain			
alternative assessment type: Non-systematic			

subjects affected / exposed	3 / 1465 (0.20%)		
occurrences (all)	3		
Pregnancy, puerperium and perinatal conditions			
Bleeding			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 1465 (0.68%)		
occurrences (all)	10		
Skin and subcutaneous tissue disorders			
Allergy			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 1465 (0.20%)		
occurrences (all)	3		
Renal and urinary disorders			
Urine retention			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 1465 (0.07%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Fracture metatarsale	Additional description: Fracture metatarsale (unrelated)		
subjects affected / exposed	1 / 1465 (0.07%)		
occurrences (all)	1		
Infections and infestations			
Infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	34 / 1465 (2.32%)		
occurrences (all)	34		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/39504520