A Pre-Market, First-In-Human, Pilot, Interventional, Clinical Investigation to Evaluate the Safety of the Aqua Therapeutics Thermal Therapy Vapor Ablation System (ATTTVAS) in premenopausal women with Abnormal Uterine Bleeding (AUB).

Published: 24-05-2024
Last updated: 07-06-2025

Primary ObjectiveTo evaluate the safety of the Aqua Therapeutics Thermal Therapy Vapor Ablation System (ATTTVAS).Secondary Objectives1. To evaluate the change of menstrual blood loss (MBL).2. To evaluate the effect of MBL on the quality of life (QoL...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Menstrual cycle and uterine bleeding disorders
Study type	Interventional research applied for the first time in human subjects

Summary

ID

NL-OMON56848

Source
ToetsingOnline

Brief title
AQTH-EA-22

Condition

- Menstrual cycle and uterine bleeding disorders

Synonym
duration, flow outside of normal volume or frequency regularity

Research involving
Human

Sponsors and support

Primary sponsor: Aqua Therapeutics, Inc.
Source(s) of monetary or material Support: Aqua Therapeutics, Inc.

Intervention

- Medical device

Keyword: Abnormal Uterine Bleeding, Endometrial ablation, Thermal Therapy Vapor Ablation System

Explanation

N.a.

Outcome measures

Primary outcome

Primary Endpoint
To evaluate the safety of the Aqua Therapeutics Thermal Therapy Vapor Ablation
System (ATTTVAS), the incidence of device-related complications will be
assessed up to the end of study.

Secondary outcome

Secondary Endpoints
1. To evaluate the change of menstrual blood loss (MBL), the pictorial blood
loss assessment chart (PBAC) score will be assessed at baseline and at End of
Study (EOS) visit.
2. To evaluate the effect of MBL on the quality of life (QoL), the Menorrhagia
Impact Questionnaire (MIQ) will be completed by the patient at baseline and at
EOS.
3. To evaluate pain intensity after treatment, a Numeric Rating Scale (NRS) *
with 0 representing no pain and 10 representing unbearable pain * will be used,
at discharge, after 24 hours and after 1 week from discharge.
4. To evaluate the procedural ease of use, a questionnaire will be completed by
the Investigator on the day of treatment.
5. To monitor menstrual changes (menstrual frequency, duration, regularity), a
menstrual calendar will be used by the patient from V-1 to EOS.
6. To evaluate the need for surgical or medical intervention to treat AUB after
EA with the ATTTVAS, any surgical or medical intervention required to treat AUB
after EA will be recorded.

7. To evaluate patient*s satisfaction with the ATTTVAS, a 5-Likert Scale will
be used at discharge and at EOS.
8. To evaluate PI*s satisfaction with the ATTTVAS, a 5-Likert Scale will be
used at discharge and at EOS.

Safety Endpoints
9. Monitoring of clinical parameters and vital signs over the duration of the
study.
10. Monitoring of device deficiencies before, during and after the use of the
device.
11. Monitoring of adverse events and serious adverse events unrelated to study
device over the duration of the study.
12. Monitoring of concomitant medications over the duration of the study.</p>

Study description

Background summary

Abnormal uterine bleeding (AUB) is defined as "flow outside of normal volume, duration, regularity, or frequency" [1]. AUB can be acute or chronic. Acute AUB is excessive bleeding that requires immediate intervention to prevent further blood loss. Chronic AUB refers to irregularities in menstrual bleeding for most of the previous 6 months [2]. AUB can be frequent or infrequent, prolonged, irregular, or heavy. Heavy menstrual bleeding (HMB) is defined as "excessive menstrual blood loss which interferes with a woman's physical, social, emotional and/or material quality of life" [2].
Causes of AUB are classified as polyps, adenomyosis, leiomyomas (AUB-L), malignancy and premalignant conditions, coagulopathy (AUB-C), ovulatory disorders (AUB-O), endometrial disorders (AUB-E), iatrogenic, and **not classified** [3]. AUB affects approximatively one in four women between 30 and 50 years of age, with serious implications on woman's quality of life (QoL) [4], [5].
Endometrial ablation (EA) is a minimally invasive, surgical treatment for women suffering from AUB. EA is a uterus-preserving procedure that aims to destroy or remove the endometrial tissue in selected women who have no desire for future fertility. The procedure was designed to treat heavy menstrual bleeding in women refractory to medical therapy (or not willing to undergo hormonal treatment) and not caused by structural uterine pathology [6]. EA has become an alternative to hysterectomy in the treatment of AUB because it is less invasive and has a shorter recovery period [7].
At present, many different techniques are available to remove the endometrial tissue. Resectoscopic endometrial ablation (REA) consists of targeted endometrial destruction under direct hysteroscopic visualization. REA techniques include endometrial laser ablation, transcervical resection of the

endometrium, and rollerball endometrial ablation [6]. Non-resectoscopic endometrial ablation (NREA) uses a variety of energy sources to non-selectively destroy the endometrial lining and include thermal balloon endometrial ablation, microwave endometrial ablation, hydrothermal ablation, bipolar radiofrequency endometrial ablation, endometrial cryotherapy, and more recently water vapor endometrial ablation [8]. NREA technologies require short surgical time and can also be performed in the outpatient setting [6].
Water vapor EA is one of the newest approaches in the field. Currently the only FDA-approved system of this kind is AEGEA Water Vapor Ablation System (AEGEA Medical, Menlo Park CA) [9].

In this context, the Aqua Therapeutics Thermal Therapy Vapor Ablation System (ATTTVAS; AQUA Therapeutics Inc.) is a novel software-controlled device designed to ablate uterine tissue using water vapor thermal therapy technology. The ATTTVAS is indicated to ablate the endometrial lining of the uterus in premenopausal women with abnormal uterine bleeding (AUB) due to benign causes for whom childbearing is complete.

In this Pre-Market, First-In-Human, Pilot, Interventional, Clinical Investigation we aim to evaluate the Safety of the Aqua Therapeutics Thermal Therapy Vapor Ablation System (ATTTVAS) in premenopausal women with AUB.

References
1. A. Khafaga and S. R. Goldstein, *Abnormal Uterine Bleeding,* Obstetrics and Gynecology Clinics of North America, vol. 46, no. 4. W.B. Saunders, pp. 595-605, Dec. 01, 2019. doi: 10.1016/j.ogc.2019.07.001.
2. V. Jain, R. R. Chodankar, J. A. Maybin, and H. O. D. Critchley, *Uterine bleeding: how understanding endometrial physiology underpins menstrual health,* Nature Reviews Endocrinology, vol. 18, no. 5. Nature Research, pp. 290-308, May 01, 2022. doi: 10.1038/s41574-021-00629-4.
3. K. A. Matteson et al., *A systematic review comparing hysterectomy with less-invasive treatments for abnormal uterine bleeding,* Journal of Minimally Invasive Gynecology, vol. 19, no. 1. pp. 13-28, Jan. 2012. doi: 10.1016/j.jmig.2011.08.005.
4. T. J. Oderkerk et al., *Endometrial ablation plus levonorgestrel releasing intrauterine system versus endometrial ablation alone in women with heavy menstrual bleeding: study protocol of a multicentre randomised controlled trial; MIRA2 trial,* BMC Womens Health, vol. 22, no. 1, Dec. 2022, doi: 10.1186/s12905-022-01843-6.
5. V. Kumar, R. Chodankar, and J. K. Gupta, *Endometrial ablation for heavy menstrual bleeding,* Women*s Health, vol. 12, no. 1. Future Medicine Ltd., pp. 45-52, Jan. 01, 2016. doi: 10.2217/whe.15.86.
6. P. Laberge et al., *Endometrial Ablation in the Management of Abnormal Uterine Bleeding,* Journal of Obstetrics and Gynaecology Canada, vol. 37, no. 4, pp. 362-376, 2015, doi: 10.1016/S1701-2163(15)30288-7.
7. P. Beelen et al., *Prognostic Factors for the Failure of Endometrial Ablation: A Systematic Review and Meta-analysis,* Obstetrics and Gynecology,

vol. 134, no. 6. Lippincott Williams and Wilkins, pp. 1269-1281, Dec. 01, 2019. doi: 10.1097/AOG.0000000000003556.
8. M. Bofill Rodriguez, A. Lethaby, M. Grigore, J. Brown, M. Hickey, and C. Farquhar, *Endometrial resection and ablation techniques for heavy menstrual bleeding,* Cochrane Database of Systematic Reviews, vol. 2019, no. 1. John Wiley and Sons Ltd, Jan. 22, 2019. doi: 10.1002/14651858.CD001501.pub5.
9. N. Leyland and M. Harris, *Water vapor endometrial ablation for heavy menstrual bleeding: 36-month follow-up of a prospective, multicenter pivotal clinical trial,* Int J Womens Health, vol. 13, pp. 169-176, 2021, doi: 10.2147/IJWH.S279864.

Study objective

Primary Objective
To evaluate the safety of the Aqua Therapeutics Thermal Therapy Vapor Ablation System (ATTTVAS).

Secondary Objectives
1. To evaluate the change of menstrual blood loss (MBL).
2. To evaluate the effect of MBL on the quality of life (QoL).
3. To evaluate pain intensity after treatment.
4. To evaluate procedure difficulty.
5. To evaluate menstrual changes (menstrual frequency, duration, regularity).
6. To evaluate the need for surgical or medical intervention to treat AUB after EA with the ATTTVAS.
7. To evaluate patient*s satisfaction with the ATTTVAS.
8. To evaluate PI*s satisfaction with the ATTTVAS.
9. To evaluate additional safety parameters.

Study design

This is a Pre-Market, First-In-Human, Pilot, Interventional, Clinical Investigation to Evaluate the Safety of the Aqua Therapeutics Thermal Therapy Vapor Ablation System (ATTTVAS) in premenopausal women with AUB.

Intervention

For each patient, a total of 6 visits (5 on-site and 1 remote) will be planned. Unscheduled visit(s) will be planned on-site according to Principal Investigator judgement.

Each Subject, after signing the Informed Consent Form (ICF), will enter a screening phase (V-1) during which several assessments (e.g., demographics, medical history, current menstrual condition, blood analysis) will be conducted.

At the screening visit, patients will receive a menstrual calendar and a PBAC to be completed. The PBAC score must be recorded as soon as available to confirm that the patient can be enrolled at baseline (PBAC must be >=150). The PBAC score will also be recorded at the End of Study (EOS) visit.
At baseline (V0) and at EOS, on site, patients will also complete the Menorrhagia Impact Questionnaire (MIQ). If the Investigator can complete all the assessments foreseen at baseline visit (V0) and V1-EA in one day, V0 and V1 may coincide.

At V1, enrolled Subjects will undergo EA with the ATTTVAS. EA must be performed within 15-20 days from the beginning of the menstrual cycle. EA cannot be performed in the presence of heavy menstrual bleeding, but it can be performed in the presence of light bleeding/spotting.
Sedation will be performed before the EA by intravenous administration of propofol and fentanyl.
The duration (seconds) of the ablation cycle will be recorded on the CRF. After the procedure is completed, the PI will fill a questionnaire on procedural ease of use. Device deficiencies (if any) will be recorded.
At discharge, after 24 hours and 1 week from discharge, patients will be asked to rate pain intensity on a Numeric Rating Scale (NRS).
At discharge patients will receive a diary to record AEs and concomitant medications through the study period.

Follow-up visits will be performed after 1 week and 6 weeks from discharge.
Satisfaction with the procedure will be evaluated using a 5-Likert Scale (completed by patient and PI) at discharge and at EOS.
Physical examination, monitoring of vital signs and AEs will be performed at each applicable visit. Current menstrual condition will be monitored during the entire study period.

To evaluate the need for surgical or medical intervention to treat AUB after EA, any surgical or medical intervention required to treat AUB after EA will be recorded during the study.

An Interim Analysis was performed on the clinical data collected from V-1 to EOS (included) for the first 5 patients enrolled. The primary aim of the interim analysis was to evaluate the safety of the medical device. During the interim analysis, the enrollment of patients stopped. The results of the interim analysis were submitted to the Ethic Committee (EC) and Competent Authority (CA). Based on the interim analysis results and, after EC/CA feedback, the study activities could continue as planned.

Study burden and risks

The expected benefits following the endometrial ablation procedure with the ATTTVAS are as follows:
- Reduction in the amount of blood lost during periods.
- Reduction in the duration of periods, or absence of blood loss between periods, or absence of periods.

After ablation surgery, it is normal to experience mild vaginal bleeding or discharge that may last for several weeks after the procedure. The most common side effects are pelvic pain, cramps, nausea, and vomiting that usually disappear within 12 to 24 hours. The serious side effects associated with the procedure include perforation of the uterus, bleeding following the procedure, retention of menstrual blood inside your uterine cavity, pelvic infections, and fever.

Contacts

Scientific
1 MED SA
Valentina Galimberti
Via Campagna 13
Agno 6982
Switzerland
+41 (0)91 605 40 50
Public
1 MED SA
Valentina Galimberti
Via Campagna 13
Agno 6982
Switzerland
+41 (0)91 605 40 50

Trial sites

Trial sites in the Netherlands

Maxima Medisch Centrum
Target size: 5

Listed location countries

Italy, Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Signed patient informed consent form (ICF).
2. Females aged >= 30 years and <= 55 years at baseline with no desire to conceive, with or without simple endometrial hyperplasia (without atypia).
3. Diagnosis of AUB.
4. Premenopausal (follicle-stimulating hormone level <= 40 mIU/mL), women who don*t want to receive hormonal treatment or who have failed to respond to hormonal treatment.
5. Pictorial Blood Loss Assessment Chart (PBAC) score >=150 at baseline.
6. Normal endometrial biopsy.
7. Negative PAP test.
8. Willingness to follow all study procedures, including attending all site visits, tests, and examinations.

Exclusion criteria

1. BMI >=35
2. Postmenopausal status.
3. Undiagnosed vaginal bleeding.
4. A patient with a history of a prior completed endometrial ablation procedure and/or endometrial resection (including endometrial ablation/resection performed immediately prior to the ATTTVAS Ablation Treatment) regardless of the modality by which it was performed.
5. Previous uterine surgery.
6. Uterine cavity-length <4 cm or >6 cm (without cervix length).
7. Not willing to avoid the use of vaginal ring, hormonal intrauterine device (concomitant IUD such as Essure is not allowed prior to the ATTTVAS Ablation Treatment), oral contraceptives during the study period.
8. Pregnant or breastfeeding.
9. Less than 1-year post-partum.
10. Any contraindication to endometrial ablation.
11. History of previous classical cesarean section or transmural myomectomy, including hysteroscopic and/or laparoscopic myomectomy performed immediately prior to the ATTTVAS Ablation Treatment.
12. Confirmed pelvic inflammatory disease, active/acute endometritis, sexually transmitted disease, bacteremia, sepsis, other active local and/or systemic infection.
13. Active genital or urinary tract infection (e.g., cervicitis, vaginitis, endometritis, salpingitis or cystitis) at the time of treatment.
14. Congenital malformation of the uterus, fibroid(s) distorting the uterine cavity, or large (> 1 cm) endometrial polyp(s).
15. Congenital malformations of the female genital tract.
16. Subjects with suspected or known coagulopathies or receiving

anticoagulation therapy.
17. A patient currently on medications that could thin the myometrial muscle, such as long-term steroid use (except for inhaler or nasal therapy for asthma).
18. Documented cervical dysplasia, complex or atypical endometrial hyperplasia, abdominal or pelvic cancer.
19. Presence of any relevant severe condition or clinically relevant abnormal laboratory parameters that in the opinion of the Investigator may interfere with the participation to the study.
20. Presence of any relevant severe organic, systemic, or metabolic disease (particularly significant history of cardiac, renal, neurological, psychiatric, oncology, endocrinology, metabolic or hepatic disease), or abnormal laboratory values that will be deemed clinically significant in Investigator*s opinion.
21. Active malignant neoplasm of any type, or history of a malignancy (patients with a history of other malignancies that have been surgically removed and who have no evidence of recurrence for at least five years before study enrollment are also acceptable).
22. Participation in another investigational study within the previous 30 days.
23. Recent history or suspicion of alcohol abuse or drug addiction.
24. Inability to follow study procedures.
25. History of allergic reactions to propofol and/or fentanyl.

Study design

Design

Study phase:	N/A
Study type:	Interventional research applied for the first time in human subjects
Intervention model:	Single
Allocation:	N/A: single arm study
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Safety

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-11-2024
Enrollment:	5

Duration:	4 months (per patient)
Type:	Actual

WORLD

Recruitment status:	Recruiting
Start date (anticipated):	30-09-2024
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medical device
Generic name:	Aqua Therapeutics Thermal Therapy Vapor Ablation System (ATTTVAS)
Registration:	No

IPD sharing statement

Plan to share IPD: No

Plan description
N.a.

Ethics review

Approved WMO

Date:	24-06-2024
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	14-08-2024
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	27-05-2025
Application type:	Amendment
Review commission:	METC AZM/UM

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84185.000.24
Research portal	NL-006018