STUDY PROTOCOL

Title: HemoDiafiltration Versus HemoDialysis in OLDER People: a Randomized, Multicenter, Crossover, Pragmatic Clinical Trial

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Protocol full title:

"HemoDiafiltration versus HemoDialysis in OLDER people: a randomized, multicenter, crossover, pragmatic clinical trial "

Protocol short title/acronym: "HD-OLDER"

Study Sponsor

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AUB Santé

HD-Older

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1. Study Synopsis

Title	HemoDiafiltration versus HemoDialysis in OLDER people: a randomized, multicenter, crossover, pragmatic clinical trial
Short title/Acronym	HD-OLDER
Study Phase	Phase 4
Sponsor Name	AUB SANTE
Principal Investigator	Dr Mabel AOUN
Data Protection Officer	Mrs Mathilde COLLET (and Mrs Sibylle GOURVIL)
ID-RCB (ANSM)	2025-A00884-45
Disease under investigation	Stage 5 chronic kidney disease on Hemodialysis
Study purpose	To determine the best modality of hemodialysis in older patients > 84 years
Study Design	Randomized, multicenter, crossover, pragmatic clinical trial. Patients will be randomized to two sequences, each one of a 3-month period. Sequence 1 includes 3 months of hemodiafiltration (Period 1) then 3 months of high-flux hemodialysis (Period 2). Sequence 2 includes 3 months of high-flux hemodialysis (Period 1) then 3 months of hemodiafiltration (Period 2).
Washout period	Two weeks of low-flux hemodialysis at the beginning of the study and between the two periods of each sequence.
Primary objective	To compare the dialysis recovery time in older patients treated with hemodiafiltration versus

	conventional high-flux hemodialysis
Secondary objectives	1.To compare the general fatigue between the two hemodialysis modalities 2. To compare symptomatic hypotension and intradialytic clotting events 3. To compare quality of life 4. To compare dialysis adequacy 5. To compare safety and adverse events
Inclusion criteria	A participant must meet ALL of the following criteria in order to participate: 1-Signed and dated informed consent 2-Age >84 years 3-Diagnosed with kidney failure 4-On maintenance hemodialysis>3 months 5-Willing to have a dialysis session of 3.5 to 4-hour duration, three times a week 6-Who has a reliable vascular access 7-Who is covered by the health insurance
Exclusion criteria	A participant who meets one of the following criteria will be excluded: 1-Patients with cognitive impairment (assessed with a mini-test if needed) 2-Hospitalized at inclusion 3-Who have difficulties with French speaking 4-Terminally ill with life expectancy<3 months 5-Active cancer
Duration of study for each participant	7 months (including 2 initial weeks of washout and 2 weeks of washout between period 1 and period 2)
Total duration of study	8-10 months
Primary Endpoint	Change in dialysis recovery time (in minutes) between the start and end of period 1 and period 2.
Secondary Endpoints	-Change in fatigue score between the start and end of period 1 and period 2.

	-Change in STS-30 between the start and end of period 1 and period 2. -Change in SF-12 scores between the start and end of period 1 and period 2. -Number of episodes of symptomatic hypotension in period 1 and period 2. -Number of intradialytic clotting events in period 1 and period 2. -Change in hemoglobin, serum albumin, potassium, phosphate and Kt/V between the start and end of period 1 and period 2. -Secondary safety endpoints: serious adverse events (death, hospitalizations).
Planned number of participants	62 patients
Statistical analysis	Analyses will be performed on an intention-to-treat basis. Baseline characteristics will be compared using the independent t-test or Mann-Whitney U test for continuous variables and Chi-Square test for categorical variables. Linear mixed models will be used to compare the outcomes.
Study Organization	Trial steering committee Scientific Advisory Board Data and Safety Monitoring Board
Ethics	The study will be conducted according to the principles of the Declaration of Helsinki 1975 and will receive the approval of the ethics committee.
Version and date of final protocol	Version 1, 14/04/2025 Version 3, 17/07/2025 Version 4, 17/09/2025

2. Abbreviations

HDF	Hemodiafiltration
HD	Hemodialysis
DRT	Dialysis Recovery Time
MCO	Medium Cut-Off
SNOSE	Sequentially numbered opaque sealed envelope
eCRF	Electronic Case Report Form

3. Schedule of activities

			Washout	Period 1		Washout	Period 2	
Visit	**Screening**	**Randomi-zation**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**
Week	**Day 0 or -1**	**Day 0**	**2 weeks**	**6 weeks**	**6 weeks**	**2 weeks**	**6 weeks**	**6 weeks**
Informed consent	X							
Eligibility criteria	X							
Demographics	X							
Comorbidities and medications	X							
Randomisation		X						
Vital signs, weight	X		X	X	X	X	X	X
Vascular access	X		X	X	X	X	X	X
Routine Laboratory before and after dialysis§	X		§	§	§	§	§	§
Concomitant medication	X		X	X	X	X	X	X
DRT question	X		X	X	X	X	X	X
Fatigue SONG-questionnaire and STS-30	X		X	X	X	X	X	X
SF-12 Health Survey	X		X		X	X		X
Dialysis specifics*	X		X	X	X	X	X	X
Serious adverse events		X	X	X	X	X	X	X

§For routine laboratory tests, they will be done monthly during Period 1 (4 times) and Period 2 (4 times) *Symptomatic intradialytic hypotension and circuit clotting will be documented each session in medical charts and the total number entered in eCRF for Period 1 and for Period 2

4. Background and rationale

4.1 Background

Patients with kidney failure, treated with hemodialysis (HD) can be offered hemodiafiltration (HDF), high-flux hemodialysis (HD) or medium cut-off (MCO) hemodialysis. HD relies on the mechanism of diffusion to epurate toxins while HDF relies on diffusion and convection mechanisms, necessitating the use of high substitution fluid replacement, and may be more effective on middle molecules clearance. Before 2023, four studies compared the survival of patients treated with hemodiafiltration versus conventional hemodialysis. A meta-analysis of these studies showed a benefit of high-dose HDF therapy [1]. In 2023, the CONVINCE trial that included 1360 patients showed better survival in patients treated with post-dilution mode HDF at a dose > 23 liters in comparison to those treated with conventional high-flux hemodialysis after a median follow-up of 30 months [2]. CONVINCE collected data on the quality of life and fatigue and showed a moderate positive effect for high-dose HDF on the cognitive function, without a significant difference on fatigue [3]. It is noteworthy that the mean age of patients included in the CONVINCE trial was 62.5 years with no data on the older category of patients >84 years old.

Dialysis recovery time has been used to assess post-dialysis fatigue and the tolerance of a dialysis session [4]. A randomized crossover clinical trial in 2017 compared dialysis recovery time between patients on HDF and conventional high-flux HD, with a mean age of 65 years, and found no difference in recovery time between the two groups but they found more episodes of symptomatic hypotension and lower serum albumin on HDF [5]. A recent observational study of our research team on fatigue and recovery time found a significant association between HDF and prolonged dialysis recovery time in a sub-group of patients >84 years old [6]. This category of age was not addressed specifically in previous studies despite the aging of the kidney failure population. Thus, it is important to find out whether HDF is less or more beneficial than conventional HD in the very elderly population.

4.2. Risks and Benefits

Risks

HDF and High-Flux Conventional HD are two dialysis modalities routinely used in clinical practice in dialysis units. There is no increased risk related to both treatments.

Benefits

One of the two modalities may reduce the fatigue experienced by elderly dialysis patients during the post-dialysis period.

5. Study Objectives and Design

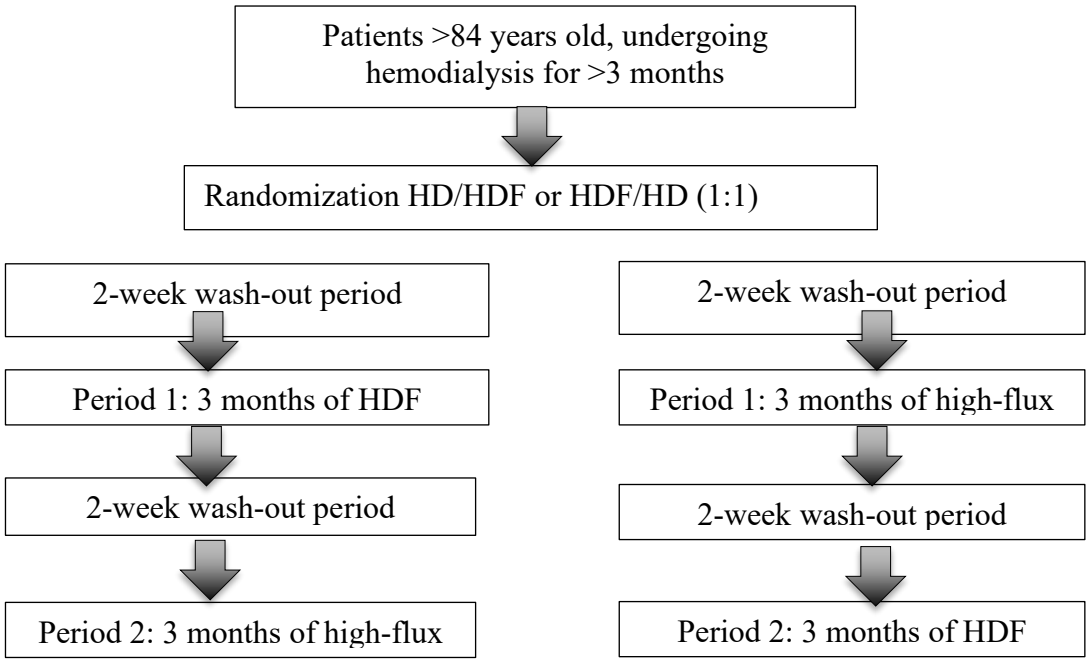
5.1. Study Objectives

The primary objective is to compare the dialysis recovery time in patients treated with HDF versus those treated with conventional high-flux hemodialysis, after 3 months of therapy. The secondary objectives are to compare the general fatigue, health-related quality of life, symptomatic intradialytic hypotension, intradialytic circuit clotting, dialysis adequacy, safety and adverse events between the two dialysis modalities.

5.2. Study design

This is a randomized, multicenter, crossover, pragmatic clinical trial. Trial-group assignments will be performed using a computer generating algorithm. Patients will be assigned to one of two sequences: HD/HDF or HDF/HD. The allocation ratio is 1:1. Allocation concealment will be ensured using SNOSE (sequentially numbered opaque sealed envelope). This is a pragmatic trial: after randomization, physicians apply the best practice and keep the same membrane during the study. Healthcare provider and patient blinding is not possible because the HDF procedure cannot be hidden. This study will assess the superiority of HDF over HD. This study will take place in 10 dialysis units in France.

5.3. Study flow chart



6. Selection and withdrawal of patients

6.1. Study setting and patient selection

Hemodialysis patients will be recruited from 10 HD centers in France.

6.2. Inclusion criteria

All patients >84 years old, with chronic kidney disease stage 5, on maintenance hemodialysis for >3 months, willing to receive 3.5 to 4-hour sessions three times per week, with a reliable vascular access, who are covered by a health insurance and who sign an informed consent, will be included.

6.3. Exclusion criteria

Patients who are hospitalized at the moment of inclusion, with cognitive impairment (assessed with a mini-Cog test if needed), active cancer patients and participants who are terminally ill defined as having an expected survival of less than 3 months, and those who difficulties in French speaking, will be excluded.

6.4. Permanent withdrawal

Participants have the right to withdraw from the study at any time for any reason. The investigator has also the right to withdraw patients from the study for medical reasons or in case of severe non-compliance. All patients who prematurely stopped should be followed for clinical events.

6.5. Duration of trial

Recruitment of patients will be done over 1-3 months or until the pre-determined sample size is reached whichever comes earlier. After randomization, the study for each participant has a duration of time of 7 months.

7. Treatment of participants

Patients who are included will receive two weeks of low-flux hemodialysis then they will receive one of two sequences:

Sequence 1 will receive HDF for three consecutive months (Period 1) then conventional high-flux HD for three consecutive months (Period 2).

Sequence 2 will receive conventional high-flux HD for three consecutive months (Period 1) followed by HDF for three consecutive months (Period 2).

Two weeks of washout with low-flux hemodialysis will be applied between the two periods (to ensure there will be no carry-over).

8. Study phases

8.1. Screening

Patients who are eligible for the study will be verbally informed about the study. After being informed, each participant should sign and date the written informed consent form, approved by the ethics committee. A screening number will be allocated to each participant using the eCRF system.

8.2. Randomization

Participants who fulfil the inclusion and exclusion criteria will be randomized in a 1:1 ratio for HDF or high-flux hemodialysis, using the SNOSE method (for allocation concealment).

8.3. Treatment phase

Baseline is defined as the beginning of each period of three months. Data will be collected and study specific activities performed based on the Schedule of Activities.

8.4. End of treatment

All patients who complete the study will undergo an end of treatment visit. Any patient who prematurely withdraws is also to be followed for safety reasons and scheduled an end of treatment visit, unless the patient refuses. At a minimum, the investigator should make all efforts to obtain information on whether or not the participant is alive or dead at the end of study.

9. Study procedures

All study activities, data collection and their timings are summarized in the Schedule of Activities. Baseline information about demographics, medical history, medications, dialysis prescription and laboratory results will be collected during routine clinical practice. All laboratory measurements will be conducted in the local laboratory of each dialysis unit. If laboratory results are not available, they should be recorded as non-available.

9.1. Data collection at screening/randomization

Eligibility criteria: clearly stated and documented in the eCRF.

Demographics: age, sex.

Comorbidities and medical history: diabetes, smoking, hypertension, hyperlipidemia, cause and date of kidney failure (dialysis vintage), previous cardiovascular disease, atrial fibrillation, Charlson score for comorbidity.

Vital signs: height and weight (dry weight). Pre-dialysis and post-dialysis systolic and diastolic blood pressure and heart rate in a sitting position will be recorded.

Dialysis prescription: Vascular access (arteriovenous fistula or graft, central venous catheter); number of dialysis hours per week; dialysis session time (morning, afternoon, evening); blood flow, dialysate flow, dialysate temperature, filter membranes (surface), dialysate potassium, sodium, calcium content and type (acetate, HCL or citrate), anticoagulation type and dose (heparin or LMWH) will be collected. Use of UF control (or profile) or Na control (or profile).

Laboratory pre-dialysis: urea, creatinine, serum phosphate, calcium, albumin, potassium, sodium, bicarbonate, hemoglobin, PTH, alkaline phosphatase, ferritin, transferrin saturation, uric acid, Kt/V (method of Kt/V assessment) to be recorded.

Laboratory post-dialysis: urea, creatinine.

Clinical variables: Urine volume will be assessed by collecting the 24 hour-urine and residual kidney function will be measured.

Medications: antihypertensive therapy: number of drugs, diuretics, renin angiotensin aldosterone system inhibitors (RAASi), CCBs, beta-blockers, alpha-blockers; antidepressants and anxiolytics. Statin, medications for diabetes, oral anticoagulant, ESA, Iron, drugs for hyperkalemia, phosphate binders, vitamin D, cinacalcet.

Dialysis recovery time (DRT) will be collected for three consecutive sessions and will be assessed by asking "*How long did it take you to recover from your last dialysis session?*"[4] or in French "*Combien de temps vous a-t-il fallu pour récupérer de votre dernière séance d'hémodialyse?*". This question will be asked by nurses to each patient at each session for three consecutive sessions at the beginning, middle and end of each period of the trial. Answers were recorded in minutes or hours.

Fatigue score will be assessed by using the French SONG-fatigue validated scale [7]. The SONG-HD fatigue scale includes three questions: *in the last week, "did you feel tired?", "did you lack energy?", "did fatigue limit your usual activities?"*. The response to these questions follows a 4-Likert scale: 0= not at all, 1=a little, 2=quite a bit, 3=severely. The total score of fatigue is defined as the sum of the three scores (0 to 9).

Stand-to-sit (STS 30) test: it is used to evaluate muscle performance and it is validated in patients on hemodialysis. It is assessed by asking the patient at the end of the session for three consecutive sessions to stand and sit on the chair as quickly as possible. The number of stand-to-sit over 30 seconds will be recorded.

Health-related quality of life will be assessed using the SF-12 quality of life score.

9.2. Data collection at follow-up

Follow-up with laboratory measurements

We will collect at baseline, one month, two months and three months of Period 1 and Period 2 the routine laboratory tests: serum urea, creatinine, phosphate, calcium, albumin, potassium, sodium, bicarbonate, hemoglobin, PTH, alkaline phosphatase, ferritin, transferrin saturation.

At the end of each period, we will collect residual kidney function.

Clinical follow-up

The number of symptomatic intradialytic hypotension episodes and of intradialytic clotting events will be documented in the patient's chart at each session and the total number will be collected at the end of each period of treatment.

Pre- and post-dialysis systolic and diastolic blood pressure will be collected at the end of each period of the trial by computing the average of the last three sessions.

Number of hospital admissions and deaths, within each period, will be collected.

Dialysis parameters follow-up

We will collect at baseline, one month, two months and three months of each period of the trial: blood flow, dialysate flow, dialysate temperature, ultrafiltration rate (mL/Kg/h), Kt/V, convective volume (for HDF), use of UF control (or profile) or Na control (or profile), dialysis session duration and time (morning, afternoon, evening).

Medications' follow-up

Any change in baseline medications to be collected every month: antihypertensive therapy, ESA, Iron, drugs for hyperkalemia, phosphate binders, vitamin D, cinacalcet.

Questionnaires

DRT question, SONG-Fatigue questionnaire, STS-30 will be administered and recorded at baseline, 6 weeks and the end of Period 1 and Period 2.

SF-12 Health Survey will be administered and recorded at baseline, and the end of Period 1 and Period 2.

10. Study Outcomes

10.1. Primary Endpoint

-Change in dialysis recovery time (in minutes) between the start and end of period 1 and period 2.

10.2. Secondary Endpoints

-Change in fatigue score between the start and end of period 1 and period 2.

-Change in STS-30 between the start and end of period 1 and period 2.

-Change in SF-12 scores between between the start and end of period 1 and period 2.

-Number of episodes of symptomatic hypotension in period 1 and period 2.

-Number of intradialytic clotting events in period 1 and period 2.

-Change in hemoglobin, serum albumin, potassium, phosphate and Kt/V between the start and end of period 1 and period 2.

-Secondary safety endpoints: serious adverse events (death, hospitalizations).

11. Assessment of safety

11.1. Safety definitions

Adverse event

An adverse event is defined as an untoward, undesirable medical occurrence after exposure to a medical product, which is not necessarily caused by that medical product.

Serious Adverse event

A serious adverse event is suspected when the outcome of the event includes death, hospitalization, disability or permanent damage and required intervention to prevent permanent impairment or damage.

Severity of adverse events

Severity should be graded as mild, moderate, severe, life-threatening or leading to death.

11.2. Relatedness

The relationship between an event and the study procedure should be assessed. Other possible causes of the event include: a worsening or change in manifestation of pre-existing/underlying disease; progression of the treated disease; causal relationship with non-study treatment or other accident or intercurrent illness.

11.3. Reporting of safety events

This study compares two modalities of hemodialysis and related adverse events are very common in both treatment modalities, thus only serious adverse events will be reported. Serious adverse events and endpoints of these events will be recorded in the participant eCRF. Pre-existing conditions and pre-planned procedures prior to the patient's inclusion are not considered serious adverse events. Any serious adverse event should be reported to the sponsor within 24 hours of the investigator learning about the event. Given that death and non-fatal hospital admissions are common and normal part of the natural course of patients with end-stage kidney disease, all reported serious adverse events and deaths will be reported to regulatory authorities every 12 months using listings.

12. Statistical methods

12.1. Sample size

Given that our previous study showed, in patients >84 years, a dialysis recovery time of 692 ± 741 minutes while using HDF and 423 ±646 minutes while using HD, if we consider a two-sided alpha of 5%, a power of 80%, the total sample size needed would be 56 patients. Assuming an attrition rate of 10%, we would need 62 patients.

The recruitment will go on until we reach this number.

12.2. Statistical analysis

Continuous variables will be presented as mean ± standard deviation (SD) if they have normal distribution, otherwise as median and interquartile (IQR). Categorical variables will be reported as numbers and percentages. Differences between the study groups will be tested using χ^2 tests (for categorical variables) and independent t test or Mann-Whitney U test for continuous variables. Linear mixed models will be used to compare the outcomes in both periods of the trial. Analysis will be performed on an intention-to-treat basis. Statistical analysis will be performed with SPSS. A P-value of ≤0.05 will be considered statistically significant.

13. Study organization

The trial steering committee is the highest decision-making body within the HD-ELDERLY study. It consists of one representative of each participating dialysis unit and is chaired by the project coordinator.

The Scientific Advisory Board will provide scientific advice concerning key project decisions and includes experts in hemodialysis from AUB SANTE.

Data and Safety Monitoring Board is an independent committee that will ensure the safety of included patients is not compromised.

14. Recording of data- sources and electronic case report forms

This study data will be captured using an eCRF. Data will be collected from the patient's medical records, questionnaires administered during the study, laboratory reports, clinical and office charts, recorded data on dialysis generators. Every investigator and research staff of each dialysis unit will have access to the eCRF in order to enter data and make changes if needed.

Only authorized staff will have access to the eCRF. Data from the eCRF will be encoded and stored in a database at the sponsor site. An electronic data trail will capture all changes made to eCRF data, with date and time of change and reason for the modifications. Upon request from the sponsor, the investigators shall provide access to any background data in the medical records, especially in case of suspicion of data transcription error. Inspection or audits may also need access to the complete study records, provided that participant confidentiality is protected.

15. Data Quality Assurance

Every investigator is responsible for ensuring eCRF data are complete and accurate. The eCRF will be reviewed regularly by a monitor from the sponsor to ensure completeness and accuracy. They can also be reviewed by the sponsor's medical staff and corrections or clarifications would be necessary. Once a patient eCRF is complete, it will be locked (data will become read-only). Each investigator will provide an electronic signature of all eCRFs of their site before the data is analyzed.

16. Data management

The content of the eCRF will be created by the principal investigator and approved by the sponsor before the start of the study. All decisions concerning the eligibility criteria of participants will be done by the research staff at the sponsor site (after discussion with the principal investigator and the scientific advisory board if necessary) and any exclusion will be documented.

17. Record retention

Each investigator at each site must retain all study records for at least two years after the publication of the study or for a longer period depending on local regulatory requirements. Patient records and other source data must be kept for at least 15 years. All records must be accessible to an audit or inspection.

18. Monitoring of the study, audits and inspections

A research staff member designated by the sponsor will visit regularly each investigator to ensure that the study is progressing in accordance with the protocol and local regulations. During these visits, the research staff will be given access to all data related to the study.

An audit may be also done at any time during or after completion of the study by the sponsor. A representative from local authorities can also inspect a study site and needs to have access to all data related to the study. The investigator of this site should contact the sponsor immediately if an inspection is taking place.

19. Data handling and confidentiality

Each investigator must assure that the participants anonymity will be maintained and their identities are protected from unauthorized parties. In eCRFs or other documents submitted to the sponsor, participants should not be identified by their names but by an identification code. The list of codes and names should be kept by each investigator. Participants written informed consents should be kept by each investigator, in strict confidence.

20. End of study, participant withdrawal and premature termination

20.1. End of study and premature termination

The steering committee has the right to terminate the participation of either a participant or a site or the study at any time. Reasons for premature termination include: a high incidence of serious adverse events, the non-adherence of an investigator to the protocol or regulatory guidelines, unsatisfactory participant enrolment, inaccurate data recording or false information.

20.2. Participant withdrawal

The reason for participant withdrawal should be recorded in the eCRF and includes one of the following: death, voluntary withdrawal, loss to follow-up, major protocol deviation, or study termination.

Participants who are hospitalized will remain in the study. Participants continuing their treatment in a non-participating dialysis unit will be considered as dropped-out. They will be followed only for mortality.

20.3. Participant replacement

No participant can be replaced after randomization.

21. Deviations and violations

A deviation is an accidental or unintentional change to, or non-compliance with the study protocol and a violation is an accidental or unintentional change to, or non-compliance with the ethics committee approved protocol without prior approval of the sponsor or the ethics committee. A deviation does not affect risks and benefits, does not have significant impact on participant's rights and safety. However, a violation generally increases risks and decreases benefits and affects the participant's rights and safety. All deviations and violations should be documented and followed up by the sponsor and reported to the regulatory authorities.

22. Ethical considerations and Protection of human participants

22.1. Regulatory authority/Ethics committee

The study will be conducted in agreement with the Helsinki Declaration of 1975 and the French laws and regulations. Approval from the ethics committee/CPP/IRB will be obtained before the study starts and will be communicated to each investigator.

The trial will be registered on ClinicalTrials.gov.

22.2. Informed consent

Every participant will give his/her written informed consent (French version, attached to the protocol), in accordance with the Declaration of Helsinki and the European data protection regulation (Règlement Européen (UE) 2016/679 du 27 Avril 2016 relatif à la protection des données personnelles (RGPD) et la loi n° 78-17 du 06 Janvier 1978 relative à l'informatique, aux fichiers et aux libertés modifiée et l'article L. 1121-1 du code de la santé publique).

The principal investigator prepares the informed consent form and submits it to the ethics committee along with the protocol for approval.

Before enrolling in the study, the investigator must provide potential participants and/or their legal representatives with an explanation of the study's objectives, methods, and potential benefits and risks. Participants will be informed that their involvement is voluntary and that they may withdraw consent at any time. They will also be assured that opting out will not affect the treatment they receive for their condition. Additionally, participants will be made aware that alternative treatments are available if they choose not to participate, and this decision will not affect their access to future treatments. Participants will be informed that a participant identification register will be maintained for potential long-term follow-up, and their medical records may be accessed by health authorities and authorized sponsor staff, in compliance with applicable laws and regulations, without compromising their confidentiality. By signing the informed consent form, participants authorize this access and consent to being contacted by their study physician for additional safety evaluations or to provide information about their vital status.

Participants will be given adequate time to read the informed consent form and have the opportunity to ask any questions. Once the explanation is provided and before entering the study, the participant's consent must be properly documented with the participant's personally dated signature and the investigator's personally dated signature. After obtaining consent, a copy of the informed consent form must be provided to the participant.

If the participant is unable to read or write, an impartial witness must be present throughout the informed consent form process, including reading and explaining all written information. The witness must personally date and sign the form after obtaining oral consent from the participant. Copies of the signed form will be given to the participant, and the original will be kept in the participant's records. If new safety information leads to significant changes in the risk/benefit assessment, the form should be reviewed and updated if needed. All participants must be informed of any new information and provide their consent to continue with the study.

22.3. Protocol amendments

Protocol amendments will be communicated to the ethics committee.

22.4. Dissemination of results

Results will be disseminated to all investigators and regulatory authorities within 3 months of the final analysis.

22.5. Insurance

The sponsor provides an insurance for participants during the period of the study, in accordance with the legal requirements. this insurance covers for damage to participants through injury or death caused by the study.

22.6. Incentives

No incentives will be given to participants.

23. References

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