REmote iSchemic condItioning in Lymphoma PatIents REceiving ANthraCyclinEs (RESILIENCE)

Published: 28-09-2023
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- to reduce the prevalence of Heart Failure (HF) in cancer survivors- to improve screening strategies for early diagnosis of anthracycline-induced cardiotoxicity (AIC)Also the following objectives:- to identify early cardiotoxicity markers- to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lymphomas non-Hodgkin's unspecified histology
Study type	Interventional

Summary

ID

NL-OMON56231

Source
ToetsingOnline

Brief title
Resilience

Condition

- Lymphomas non-Hodgkin's unspecified histology
- Lymphomas non-Hodgkin's unspecified histology

Synonym
lymphoma, Non Hodgkin Lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC)
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: anthracyclines, cardiac toxicity, Non Hodgkin Lymphoma

Outcome measures

Primary outcome

Absolute change in LVEF (between baseline and any follow-up CMRs, whichever shows worse LVEF).

Secondary outcome

Rate of anthracycline-induced cardiotoxicity events (based on drop in LVEF between baseline and any CMR of the 2 follow-up CMRs, whichever shows lower LVEF).

Cardiotoxicity event is defined as one of the following:

- Drop in LVEF between study CMRs of >=10 absolute points regardless the absolute value of follow- up ejection fraction (EF).

- Drop in LVEF between study CMRs of >=5 to <10 absolute points with a follow-up EF value <50%

Rate of atrial fibrillation.

Rate of hospital admission for sustained ventricular tachycardia, ventricular fibrillation (VT/VF) or resuscitated cardiac arrest.

Time to all cause death

Time to HF hospitalization

Rate of tumour regression.

Change in Quality of Life (QOL, scores in questionnaires) between baseline and

2 time-points (after 3rd chemotherapy cycle, and 9 weeks after the last

chemotherapy cycle).

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Study description

Background summary

See page 13-16 of the studyprotocol:
Very recent data show that >35% of patients receiving anthracyclines develop any form of cardiotoxicity. More importantly, 6% of all patients receiving anthracyclines (200.000 patients every year in Europe) develop moderate to severe cardiotoxicity.
There is an unmet need to identify therapies for cancer patients undergoing anthracycline regimes that can reduce the burden of chronic HF in this vulnerable population.

Remote ischemic conditioning is a safe and cheap intervention that has been shown to prevent anthracycline-induced cardiotoxicity in a preclinical model. Remote ischemic pre-conditioning (RIC) is a phenomenon by which brief, reversible episodes of ischemia followed by reperfusion in one organ (e.g. an arm) render remote tissues and organs resistant to injury.
RIC is safe and effective, non-invasive, easily feasible, and inexpensive intervention, which has been mainly tested in the context of myocardial infarction and stroke.
Recent evidence suggests that, to be protective, RIC has to be initiated before the index insult. This is thus the ideal setting for AIC since the chemotherapy is a planned procedure.

NHL is one of the most common cancer types in Europe, with 115,000 new cases diagnosed every year, and it is predicted that these figures will rise in the close future. Most NHL cases require a combination chemotherapy including anthracyclines.

Study objective

- to reduce the prevalence of Heart Failure (HF) in cancer survivors

- to improve screening strategies for early diagnosis of anthracycline-induced cardiotoxicity (AIC)

Also the following objectives:
- to identify early cardiotoxicity markers
- to validate a novel ultrafast CMR sequence

Study design

- study phase: phase II
- study type: interventional
- double-blinded, sham-controlled, randomized clinical trial
- primary purpose: to evaluate the efficacy and safety of Remote Ischaemic Conditioning (RIC) and validation of the novel ultrafast CMR sequence
- Number of Arms: 2
- Randomization (1:1) will be stratified by LVEF on baseline CMR (as quantified by CMR core lab /CNIC), by research Centre and by patient*s gender.

Patients enrolled undergo baseline Cardiac Magnetic Resonance (CMR), and high sensitivity troponin (hsTn) and NT-proBNP blood test.
Patients with confirmed LVEF >40% by CMR will be randomized 1:1 to RIC vs simulated RIC (Sham).
After the 3rd chemotherapy cycle, a second CMR+ hsTn/ NT- proBNP will be performed for the validation of the early marker of cardiotoxicity.

A third hsTn/ NT-proBNP blood test will be performed in the last chemotherapy cycle.

9 weeks after finishing chemotherapy, the last CMR+ hsTn/ NT-proBNP will be performed.

Patients will be followed-up for clinical events at 6, 12, 18, 30 and 42 months until the last patient undergoes the final CMR.
When the last patient undergoes the last CMR, the follow-up will be closed.
The median follow-up estimation for clinical endpoints is 24 months (range: 6 to 42 months).

Recruitment period: 36 months.
Minimum follow-up of all patients: 9 weeks after the last chemotherapy cycle (approx. 6 months after recruitment)
Maximum follow-up: 36 months after the last chemotherapy cycle.

Intervention

Intervention is RIC vs simulated RIC (Sham)

The procedure will be performed by using an electric auto-control device for remote ischemic conditioning (RIC) or simulated RIC (Sham) in the upper limb.

Patients will undergo a RIC/Sham session at home every week during the entire duration of chemotherapy (last session one week after the last chemotherapy cycle).

The first RIC/Sham session will be performed at the hospital immediately before the first chemotherapy cycle.
In addition to weekly home session, each time the patient comes to receive chemotherapy, a RIC/Sham session will be performed in the hospital immediately before starting the cycle.

If the same day of weekly home therapy coincides with the chemotherapy cycle, the home session will not be performed.
In all other cases, the week they receive the chemotherapy cycle, the patient will undergo 2 sessions of RIC/Sham (at home as scheduled plus the day of the chemotherapy cycle).

Study burden and risks

- The RIC/Sham technique is a safe and well-tolerated procedure,but it may be associated with some mild-moderate harmful events like: tingling, redness of skin, pins and needles, skin marking, pain, uncomfortable, numbness, tightness and swelling fingers or hand, loss of sensitivity or inability to move the upper arm, forearm, and/or hand, wrist drop or deficiency to extend the wrist, petechiae or hematoma.

- Quality of life is part of this trial. This could be experienced as a burden.

- There may be some discomfort from the measurements during the study,:
- collection of blood: the subject may experience bruising or irritation at the site where the needle enters the skin. Some patients may faint and, in
rare cases, get an infection.
- CMR scan: There are no known risks or side effects of a CMR scan. If a contrast agent is used, the investigator will inform the subject of possible side effects or an allergic reaction.
- ECG (electrocardiogram): There is usually no risk associated with undergoing an ecg. The stickers may pull on the subject's skin or cause redness or itching.

- Participating in the study will cost extra time

- Patients have to comply with the study agreements.

Contacts

Public
Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC)

Melchor Fernández Almagro 3
Madrid 28029
ES
Scientific
Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC)

Melchor Fernández Almagro 3
Madrid 28029
ES

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- >=18 years old
- First NHL diagnosis
- Scheduled to undergo >=5 chemotherapy cycles including anthracyclines
.Pre-chemo LVEF >40% on screening echocardiography.
- Presence of >=1 of the following risk factors for developing cardiotoxicity:
o Previous coronary artery disease without evidence of prior myocardial infarction (any of the following):
* Previous coronary revascularisation (PCI or CABG)
* Medical history of previous significant non-revascularized coronary stenosis

o LVEF 41-54%
o Age >= 65 years old
o Previous diagnosis of arterial hypertension (with or without treatment)
o Chronic kidney disease (estimated glomerular filtration rate < 60ml/min/1.73m2)
o Current or former smoker.
o Obesity (BMI>=30 kg/m2)
o LVH on screening echocardiography (LV thickness >=12mm).
o High alcohol intake (>=21 alcoholic beverages per week)
- Sinus rhythm on screening ECG

Exclusion criteria

- History of any of the following diseases:
o Any cancer who received anthracyclines treatment before the index episode
o Previous clinical diagnosis of heart failure.
o Previous diagnosis of acute myocardial infarction.
o Permanent atrial fibrillation (AF).
o Severe valvular or sub-valvular heart disease, either as a previously clinical diagnosis or as a finding on screening echocardiography.
o Severe peripheral arterial disease in the upper extremities or arteriovenous (AV) shunt in the arm selected for RIC.
- Clinical diagnosis of diabetes, with or without treatment.
- Contraindication for contrast enhanced CMR
- Severe thrombocytopenia (platelet <50) on any blood test within the previous 3 months.
- Patients participating in other randomized clinical trials.
- Impossibility to consent or undergo study follow-ups

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-12-2024
Enrollment:	70
Type:	Actual

Medical products/devices used

Generic name:	RIC device
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Date:	28-09-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL83331.000.23