ISRCTN55050065 https://doi.org/10.1186/ISRCTN55050065

Modulators of telomerase activity

Submission date
05/02/2016

Recruitment status
No longer recruiting

Registration date
16/02/2016

Overall study status
Completed

Last Edited
18/10/2016

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The cells in the human body contain DNA, complex chemical that carries genetic information. DNA is made up of small, 'X' shaped structures which are responsible for specific genes (chromosomes). At the ends of the chromosomes are stretches of DNA called telomeres, which protect the genetic material by preventing the DNA from fraying and unravelling, like the plastic tips on the end of shoe laces. As cells reproduce (copy themselves into two identical cells), the telomere caps become shorter, which is linked with the process of aging (at a cellular level). When the telomeres become too short to do their job properly, the cells can no longer divide and so becomes inactive (senescent) or dies. This shortening process is associated with aging, cancer, and a higher risk of death. Recent studies have shown that there is a connection between the processes of telomere shortening and the development of cardiovascular disease (disease of the heart and blood vessels). Telomerase is a protein which can help to prevent telomere shortening by lengthening telomeres in certain types of cells. By increasing the activity of telomerase, it could be possible to help slow down cellular aging, and prevent the development of diseases such as cardiovascular disease. The aim of this study is to find out whether atorvastatin (a cholesterol lowering drug) and perindopril (a blood pressure lowering drug) can help to increase telomerase activity in patients with high cholesterol and high blood pressure with no signs of significant cardiovascular disease.

Who can participate?
Adults aged between 35 and 75 years with high cholesterol can take part in part one and adults aged between 35 and 75 years with high blood pressure and no known diabetes or heart disease can take part in part two.

What does the study involve?
In part one of the study, 100 participants with high cholesterol are randomly allocated to one of two groups. Those in the first group are treated with 20mg atorvastatin every day for 12 months. Those in the second group do not receive any medication for the two months of the study. In part two of the study, 52 participants with high blood pressure are randomly allocated to one of two groups. Those in the first group are treated with 5-10mg of perindopril daily for 12 months as well as any diuretics (water tablets) needed to control their blood pressure (if necessary). Those in the second group are treated using standard medications used to treat high

blood pressure for 12 months. At the end of the study, participants in both groups of each part of the study have blood and urine samples taken so that they can be assessed in the lab for signs of telomerase activity.

What are the possible benefits and risks of participating?
There are no direct benefits to participants. There is a small risk that participants may experience pain and bruising following blood tests.

Where is the study run from?
National Research Center for Preventive Medicine, Ministry of Healthcare of Russian Federation (Russia)

When is the study starting and how long is it expected to run for?
February 2013 to March 2015

Who is funding the study?
Ministry of Healthcare of Russian Federation (Russia)

Who is the main contact?
Dr Irina Strazhesko

Contact information

Type(s)
Scientific

Contact name
Dr Irina Strazhesko

ORCID ID
https://orcid.org/0000-0002-3657-0676

Contact details
Federal State Institution "National Research Center for Preventive Medicine" of the Ministry of Healthcare of the Russian Federation
bld. 10
Petroverigskiy lane
Moscow
Russian Federation
1010000
+7 (0)985 210 73 27
istrazhesko@gmail.com

Additional identifiers

Protocol serial number
01201251133

Study information

Scientific Title
Effect of atorvastatin therapy and perindopril therapy on telomerase activity in patients free of cardiovascular diseases

Study objectives
Twelve months of statin therapy or perindopril therapy increases telomerase activity in peripheral blood mononuclear cells.

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Research Center for Preventive Medicine, 13/03/2013, ref: 06-03-14

Primary study design
Interventional

Study design
Single-centre randomised controlled trial with two sub-study arms

Study type(s)
Treatment

Health condition(s) or problem(s) studied
1. Hypercholesterolemia
2. Hypertension

Interventions
Part one - Atorvastatin arm:
Participants are randomized (using of a table of random numbers) to one of two groups in a 1:1 ratio.

Intervention group: Participants receive 20mg atorvastatin daily for 12 months.
Control group: Participants do not receive any additional medication in the 12 month study period.

Part two - Perindopril arm:
Participants are randomised (using of a table of random numbers) to one of two groups in a 1:1 ratio.

Intervention group: For 12 months participants receive 5-10 mg of perindopril once or twice a day as monotherapy or in combination with diuretics to achieve target levels of blood pressure.
Control group: For 12 months participants receive other antihypertensive drugs: beta-blokers, calcium antagonists, diuretics to achieve target levels of blood pressure. In this group inhibitors of renin-angiotensin-aldosterone system are prohibited.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
1. Atorvastatin 2. Perindopril

Primary outcome(s)
Telomerase activity, measured by quantitative polymerase chain reaction at 12 months

Key secondary outcome(s)
1. Markers of chronic inflammation (C-reactive protein, fibrinogen, interleukin 6), measured using blood analysis at baseline and 12 months
2. Blood urea, measured using uranalysis at baseline and 12 months
3. Carotid-femoral pulse wave velocity, measured using SphygmoCor at baseline and 12 months
4. Intima-media thickness and atherosclerotic plaques number, measured using ultrasonography with PHILIPS iU22 ultrasound system at baseline and 12 months
5. Flow dependent vasodilation, measured by probe with reactive hyperemia at baseline and 12 months

Completion date
02/03/2015

Eligibility

Key inclusion criteria
All participants:
Aged 35 to 75 years

Atorvastatin arm:
1. Diagnosed with hypercholesterolemia (low-density lipoproteins cholesterol [LDL-C] ≥160 mg /dL (4.16 mmol/L) in the presence of 0–1 CVD risk factors and LDL-C ≥130 mg/dL (3.38 mmol/L) in the presence of two or more CVD risk factors
2. Absence of any lipid-lowering therapy at the time of inclusion

Perindopril arm:
1. Hypertension grade 1-2

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Key exclusion criteria
1. Any chronic somatic diseases, including CVD associated with atherosclerosis, grade 3 hypertension, chronic heart failure (NYHA III–IV), chronic kidney disease (glomerular filtration rate <60 mL/min/1.73m2), liver disease, type 2 diabetes mellitus, acute and chronic

inflammatory diseases, cancer, pregnancy, lactation
2. Refusal to participate in the study

Date of first enrolment
05/04/2013

Date of final enrolment
16/08/2013

Locations

Countries of recruitment
Russian Federation

Study participating centre
National Research Center for Preventive Medicine
Ministry of Healthcare of Russian Federation
Petroverigskiy lane, bld. 10
Moscow
Russian Federation
101990

Sponsor information

Organisation
Ministry of Healthcare of Russian Federation

ROR
https://ror.org/01p8ehb87

Funder(s)

Funder type
Government

Funder Name
Ministry of Healthcare of Russian Federation

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	30/09/2016		Yes	No