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The effectiveness of atorvastatin for deep vein thrombosis prevention in cancer patients undergoing chemotherapy

Submission date
15/12/2020

Recruitment status
No longer recruiting

Registration date
17/12/2020

Overall study status
Completed

Last Edited
25/03/2025

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Venous thromboembolism (VTE) is a condition in which a blood clot forms in the deep veins of the leg, groin or arm and travels in the blood circulation. The incidence of VTE is increased in cancer patients and even more in patients who undergo chemotherapy. Most occur right after the chemotherapy is started.
VTE is a leading cause of increased death and illness, delay of care, and economic burden in cancer patients. One of the most common VTEs is deep vein thrombosis (DVT) and there is a three times higher risk of death in patients with asymptomatic DVT.
Previous studies have proven the effectiveness and safety of thrombo-prophylaxis (preventing the formation of blood clots) in medically ill and cancer patients, so a recommendation for this has been made for clinical practice. However, there are still a lot of clinicians not using thrombo-prophylaxis in daily use, the most common reasons are the cost, bleeding risk, and lack of knowledge, confidence, and awareness to use an anticoagulant drug as thrombo-prophylaxis.
The immune system and inflammation have long been recognized as playing roles in cancer-related VTE. Statins have an anti-inflammatory effect so might have a benefit with a lower bleeding risk, lower cost, and easier use compared to conventional anticoagulants. There is still limited data about statins and their role in preventing VTE cancer patients who undergo chemotherapy still needs to be confirmed.
Rivaroxaban is an anticoagulant with a relatively convenient use, a single dose orally daily. A previous study has proven that rivaroxaban could reduce thrombosis events with a low bleeding risk. Rivaroxaban also does not need daily coagulation monitoring.
The study aims to compare the effectiveness of atorvastatin and rivaroxaban for DVT prevention, inflammation and coagulation in cancer patients who have a high risk of thrombosis while undergoing chemotherapy.

Who can participate?
Patients aged 18-60 with cancer and no previous chemotherapy

What does the study involve?
Participants are randomly allocated to take either atorvastatin or rivaroxaban daily for 3 months

for DVT prevention. Participants are assessed with Doppler ultrasonography at the start of the study and after 3 months.

What are the possible benefits and risks of participating?
The researchers think that atorvastatin will be as effective as rivaroxaban in DVT prevention but at a lower cost. The common side effects of atorvastatin are increased liver function tests, myopathy, joint pain, and muscle weakness. However, these side effects are usually well-tolerated and severe adverse events are rarely found. The most common side effect of rivaroxaban is bleeding in the gums, skin and with urinating or defecating. Participants will be monitored for the adverse events and will be treated.

Where is the study run from?
Dr. Kariadi Hospital (Indonesia)

When is the study starting and how long is it expected to run for?
November 2020 to March 2022

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Budi Setiawan
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number
BS-VTE-001

Study information

Scientific Title
Comparing the effectiveness between the use of atorvastatin and rivaroxaban for deep vein thrombosis prophylaxis, inflammatory responses, and coagulation activities in cancer patients who have a high risk of thrombosis while undergoing chemotherapy: focus on IL-6, CRP, TF, F1+2, D-dimer, NF-kB, and TNF-alpha serum level and Doppler ultrasonography

Study objectives
1. Atorvastatin 20 mg administration for 3 months can be used as an alternative for thrombo-prophylaxis in cancer patients who have a high risk of thrombosis while undergoing chemotherapy
2. Atorvastatin 20 mg is as effective as rivaroxaban and has better cost-effectiveness for thrombo-prophylaxis in cancer patients who have a high risk of thrombosis while undergoing chemotherapy
3. Atorvastatin 20 mg administration for 3 months is not inferior compared to rivaroxaban as a thrombo-prophylaxis in cancer patients who have a high risk of thrombosis while undergoing chemotherapy
4. Atorvastatin 20 mg administration for 3 months will reduce the IL-6, CRP, TF, F1+2, D-dimer, NF-kB, and TNF-alpha serum level and reduce DVT incidence measured by Doppler ultrasonography

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/11/2020, Health Research Ethics Committee RSUP Dr. Kariadi Semarang (Sutomo St no. 16, Indonesia; +62 (0)24 8413476; kepk.rskariadi@gmail.com), ref: 665/EC/KEPK-RSDK /2020

Study design
Single-center interventional double-blinded randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of deep vein thrombosis in cancer patients who have high risk of thrombosis while undergoing chemotherapy

Interventions

Participants who meet the inclusion criteria will be randomized with simple randomization into the study group (atorvastatin 20 mg daily orally) or the control group (rivaroxaban 10 mg daily orally) for 3 months.

At baseline Doppler ultrasonography is performed on the lower extremities; IL-6, CRP, TF, F1+2, D-dimer, NF-kB and TNF-alpha serum levels are measured and re-measured after 3 months.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Atorvastatin, rivaroxaban

Primary outcome(s)
Deep vein thrombosis event measured using Doppler ultrasonography at baseline and 3 months

Key secondary outcome(s))
1. IL-6 is measured using ELISA at baseline and 3 months
2. NF-kB is measured using ELISA at baseline and 3 months
3. CRP is measured using a spectrophotometer at baseline and 3 months
4. TF is measured using ELISA at baseline and 3 months
5. F1+2 is measured using ELISA at baseline and 3 months
6. D-dimer is measured using ELISA at baseline and 3 months
7. TNF-alpha is measured using ELISA at baseline and 3 months
8. Cost effectiveness is measured using the total cost for each subject

Completion date
28/02/2022

Eligibility

Key inclusion criteria
1. Cancer patient with a definite diagnosis of cancer based on anatomy pathological examination
2. Cancer patients who have not received any chemotherapy
3. Khorana risk score ≥2
4. Age 18-60 years old
5. Has signed the participant agreement

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Total final enrolment
86

Key exclusion criteria
1. Deep vein thrombosis diagnosed with Doppler ultrasonography examination at baseline
2. Within 14 days post-surgery
3. Pregnancy
4. Taking an anti-thrombotic drug
5. Congenital altered coagulation system
6. Creatinine clearance <30 ml/minute
7. Patients with AST level >3x upper normal limit
8. Patients with total bilirubin total >5 mg/dl
9. Patients with CK >3 x upper normal limit
10. Performance status ECOC ≥3
11. Patients with cardio-cerebrovascular disease
12. Patients with infection
13. Patients with active, major, serious, life-threatening bleeding that can not be overcome with medical or surgical intervention, esp in a critical area (intra-cranial, pericardial, retroperitoneal, intra-occular, intra-artikular, intraspinal)
14. Malignant hypertension
15. Congenital coagulopathy or severe platelet dysfunction
16. Severe and persistent thrombocytopenia (<20,000/µl)

Date of first enrolment
04/01/2021

Date of final enrolment
30/11/2021

Locations

Countries of recruitment
Indonesia

Study participating centre
Dr. Kariadi Hospital
Sutomo St, no. 16
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Sponsor information

Organisation
Dr. Kariadi Hospital

ROR
https://ror.org/040f86t49

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
Current individual participant data (IPD) sharing statement as of 21/02/2022:
The data sets generated during and/or analysed during the current study are/will be available upon request via email to Budi Setiawan (boedhi_smg73@yahoo.com) when the data will become available. The raw data will be available for 2 years.

Previous individual participant data (IPD) sharing statement:
The datasets generated during and/or analysed during the current study are/will be available upon request (please email your request to boedhi_smg73@yahoo.com, Budi Setiawan).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Primary efficacy end point	08/05/2023	09/05/2023	Yes	No
Results article	Secondary outcome results	19/03/2025	25/03/2025	Yes	No
Participant information sheet	Participant information sheet	16/12/2020	22/12/2020	No	Yes
Participant information sheet		11/11/2025	11/11/2025	No	Yes
Preprint results		21/10/2022	27/10/2022	No	No
Protocol file			23/08/2022	No	No