# Platelet RNA profiling to screen for cancer in patients with unprovoked venous thromboembolism

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Miscellaneous and site unspecified neoplasms malignant and unspecified |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON47931

**Source**
ToetsingOnline

**Brief title**
Tumour-educated platelets in venous thromboembolism

### Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified
- Embolism and thrombosis

**Synonym**
venous thromboembolism; thrombosis

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** occult cancer, platelet RNA, screening, venous thromboembolism

## Outcome measures

### Primary outcome

An adjudicated diagnosis of solid or haematological cancer which is confirmed by histology or cytology, or is unequivocally diagnosed by either imaging or tumour markers.

### Secondary outcome

- Early-stage solid cancer, defined as stage I or II solid cancer according to the AJCC criteria.
- Solid cancer
- Hematological cancer
- Solid cancer and lymphoma
- Recurrent venous thromboembolism
- Major bleeding
- Clinically relevant non-major bleeding
- All-cause mortality
- Cancer-related mortality

# Study description

### Background summary

Cancer induces a hypercoagulable state which results in a 4- to 7-fold increased risk of deep vein thrombosis or pulmonary embolism, collectively

termed venous thromboembolism (VTE), compared to patients without cancer.5 Conversely, VTE may be the first sign of a cancer that has not yet become clinically overt, i.e. occult cancer. Particularly when VTE develops in the absence of identifiable risk factors, i.e. unprovoked VTE, the risk is high. Contemporary studies report a risk of 4% to 6% among patients with unprovoked VTE within the first 12 months following the VTE diagnosis.
Over the past decades, many different approaches to screen for occult cancer in patients with unprovoked VTE have been evaluated. These aim at early cancer diagnosis to reduce cancer-related morbidity and mortality. Screening strategies are often classified as either *limited* or *extensive*, wherein limited screening usually consists of at least a thorough medical history and physical examination, basic blood work-up, and a chest X-ray. The extensive screening strategies commonly extend the limited work-up by, for example, imaging (e.g. CT abdomen or whole-body PET-CT) or tumour markers (e.g. PSA, CEA, or CA-125).

Recently, the Canadian SOME trial compared a limited screening strategy with limited screening plus extensive abdominal CT in 854 patients with unprovoked VTE.1 CT-scanning of the abdomen included a virtual gastroscopy and colonoscopy, biphasic liver scan, pancreatogram and uniphasic bladder scan. Patients were followed for 12 months. Overall, cancer was detected in 14 of 431 patients (3.2%) allocated to limited screening and 19 of 423 (4.5%) patients allocated to extensive screening (P=0.28). The proportion of these cancers that were missed by the initial screening was 4 of 14 (28%) in the limited screening group and 5 of 19 (26%) in the extensive screening group (P=1.0). The authors concluded that CT-based extensive screening does not have a benefit over limited screening. Based on these results, limited screening for cancer in patients with unprovoked VTE is now considered standard of care in most parts of the world.

Despite advances in diagnostic techniques, limited screening still misses a substantial proportion of cancers in patients with unprovoked VTE. Contemporary studies have reported sensitivities of only 40% to 70%. Given the huge and often fatal impact of a late cancer diagnosis, there is an urgent clinical need to improve occult cancer detection in patients with unprovoked VTE.
Recently, platelet RNA profiling has been introduced as a novel biomarker for cancer diagnosis.4 Confrontation of platelets with tumor cells results in an altered RNA signature of platelets via transfer of tumor-associated biomolecules. These platelets are then designated as *tumour-educated platelets*. This RNA profile of tumour-educated platelets appears to be fundamentally different from the profile of healthy donors allowing for its use as a pan-cancer diagnostic tool. In a study of 228 patients with various cancers and 55 healthy donors, platelet RNA profiling was associated with a sensitivity of 96% and a specificity of 92% for detecting cancer. In addition, the platelet RNA profile was able to indetify the most likely tumor type with considerable accuracy, correctly classifying cancer patients in 50% to 75% of cases. This promising, novel technique appears to have a high discriminatory

performance, but needs external validation in target populations before clinical application.

### Study objective

The primary objective of the present study is to evaluate the accuracy of platelet RNA profiling for occult cancer detection in patients of 40 years or older with a first episode of unprovoked VTE, in an investigator-initiated, multinational, prospective, observational, cohort study.
Secondary objectives of the present study include evaluation of a novel approach proteomic analysis and circulating tumor DNA assay for occult cancer detection and evaluation of biomarker-based risk scores for bleeding and recurrent VTE.

### Study design

Investigator-initiatied, multinational, observational, prospective cohort study

### Study burden and risks

The burden for patients consists of blood withdrawals at day 1 (32ml) and day 90 (12 ml), and a structured interview for signs and symptoms of cancer, recurrent VTE, and bleeding at days 90 (15 min, clinic visit), 180 (10 min, by phone), and 365 (10 min, by phone). A telephone visit at 24 months will be scheduled for those who consented for additional follow-up visits.

There are no risks for participants. There is no expected benefit for patients.

## Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

- First, objectively confirmed, symptomatic, unprovoked symptomatic pulmonary embolism and/or distal or proximal deep vein thrombosis of the leg
- Age 40 years or older
- Written informed consent

## Exclusion criteria

- One or more of the following risk factors for veneuze trombo-embolie (VTE):
- known malignant disease prior to VTE defined as a cancer diagnosis or cancer treatment within the past 5 years;
- trauma or fracture of the leg, surgical procedures, general anesthesia, or immobilization greater than 3 days within previous 3 months;
- previous unprovoked venous thromboembolism;
- known hereditary or acquired thrombophilia;
- current pregnancy or puerperium (up to 3 months postpartum);
- current estrogen therapy.
- Greater than 10 days after VTE diagnosis;
- Inability for blood withdrawal at baseline;
- Inability or refusal to provide written informed consent

# Study design

## Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 27-06-2016 |
| Enrollment: | 270 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 09-06-2016 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 21-06-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 17-08-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-10-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 26-03-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

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| Approved WMO Date: | 13-01-2020 |
| Application type: | Amendment |
| 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 | NL57256.018.16 |