# Anticoagulation in patients with brain cancer: an international registry

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DOACs are non-inferior to LMWH with regard to the risk of ICH in patients with brain cancer requiring anticoagulation.

| | |
|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving gestart |
| **Type aandoening** | - |
| **Onderzoekstype** | Observationeel onderzoek, zonder invasieve metingen |

## Samenvatting

### ID

NL-OMON19911

**Bron**
NTR

**Verkorte titel**
ABC Registry

**Aandoening**

Metastatic brain cancer is defined as a pathology report confirming systemic solid cancer and an imaging report confirming brain metastases.

Primary brain tumors will be defined as a pathology report documenting aggressive glioma (anaplastic oligodendroglioma, anaplastic Astrocytoma, glioblastoma multiforme) or primary CNS lymphoma.

Active brain cancer will be defined as newly diagnosed brain cancer and/or active anti-cancer therapy and/or a progressive metastastic disease, at study index.

Anticoagulation is defined as treatment with either DOACs or LMWH for any indication or treatment duration. Therapeutic doses include full therapeutic doses, as well as indicated dose-reductions prescribed with therapeutic intent.

### Ondersteuning

**Primaire sponsor:** Amsterdam UMC - location AMC

**Overige ondersteuning:** None

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

Major, non-traumatic ICH at 12 months after study index.

# Toelichting onderzoek

### Achtergrond van het onderzoek

Patients with malignancy are at risk of developing cardiovascular complications which warrant anticoagulation, including venous thromboembolism (VTE) and atrial fibrillation (AF), with the former being especially prevalent in brain cancer. Anticoagulation in cancer patients is associated with an increased bleeding risk, particularly ICH. This increased risk of ICH with anticoagulation has been demonstrated in patients with high-grade glioma, but is yet to be confirmed in patients with metastatic brain cancer. There are scarce data on predictors of ICH in patients with brain cancer receiving anticoagulation. The PANWARDS score was not developed for cancer patients, but has been assessed in this setting with conflicting results. Over the past decade and a half, low-molecular-weight heparin (LMWH) has been the standard anticoagulant in cancer patients with VTE, and accordingly most of the above data relates to LMWH treatment. Direct oral anticoagulants (DOACS) have recently become an alternative for treatment of cancer-associated thrombosis, but limited data exists regarding the safety of DOACs in patients with brain cancer. Two recent retrospective studies conducted by our groups have shown similar rates of ICH with LMWH and DOACs in patients with metastatic brain cancer. Rates of ICH in patients with primary brain tumors treated with DOACs (0 of 20 patients; 0%) were remarkably low, compared with LMWH (17 of 47 patients; 36.2%) in one of these cohorts, while the other demonstrated similar ICH rates, albeit with an even smaller sample. This data should be viewed as hypothesis-generating since the samples were small and confidence intervals were wide (e.g. HR 0.57; 95% CI 0.12-2.87 for major ICH with DOAC vs. LMWH in metastatic brain cancer). Although anticoagulation-related ICH is frequent in these patients, data on management (e.g. use of hemostatic/reversal agents and restarting anticoagulation) are scarce and outcomes appear to be poor. The lack of a definition for anticoagulation-associated ICH validated against clinical outcomes, hampers research in this field.
Accordingly, the following knowledge gaps remain: 1) ICH rate with DOACs in patients with brain cancer; 2) predictors of ICH in patients with brain cancer receiving anticoagulation; 3) Management and outcomes of anticoagulation-related ICH; 4) Validation and implementation of clinically relevant definitions of ICH.

**Doel van het onderzoek**

DOACs are non-inferior to LMWH with regard to the risk of ICH in patients with brain cancer requiring anticoagulation.

**Onderzoeksopzet**

Study index will be defined as the first day of concurrent anticoagulation and diagnosed brain cancer, and patients will be followed for 12 months.
Patients with anticoagulation-related ICH will be followed for an additional 90 days post ICH.
Patients will be censored upon death, or migration/loss to follow-up and those discharged to receive terminal care will be considered deceased at the date of the last contact.

**Onderzoeksproduct en/of interventie**

N/A

# Contactpersonen

## Publiek

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## Wetenschappelijk

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# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1) Active high-grade glioma or confirmed presence of brain metastases
2) DOAC or LMWH prescribed at therapeutic doses in the presence of active brain cancer, for

any indication and any duration
3) At least two neuroimaging studies (computed tomography (CT) or magnetic resonance imaging (MRI)) from index day until the end of 12-month follow-up, unless death occurs first.

### Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1) Intracranial hemorrhage before initiation of anticoagulation
2) Lack of follow-up data

## Onderzoeksopzet

### Opzet

| | |
|---|---|
| Type: | Observationeel onderzoek, zonder invasieve metingen |
| Onderzoeksmodel: | Anders |
| Toewijzing: | Niet-gerandomiseerd |
| Blindering: | Open / niet geblindeerd |
| Controle: | Geneesmiddel |

### Deelname

Nederland

| | |
|---|---|
| Status: | Werving gestart |
| (Verwachte) startdatum: | 01-01-2015 |
| Aantal proefpersonen: | 2200 |
| Type: | Verwachte startdatum |

### Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Ja

## Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 23-10-2020 |
| Soort: | Eerste indiening |

# Registraties

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

| Register | ID |
|---|---|
| NTR-new | NL8995 |
| Ander register | METC AMC : W19_261 # 19.312 |

# Resultaten

**Samenvatting resultaten**

Leader A, Hamulyák EN, Carney BJ, et al. Intracranial Hemorrhage with Direct Oral Anticoagulants in Patients with Brain Metastases [abstract]. Res Pr Thromb Haemost. 2020;4(Suppl 1). https://abstracts.isth.org/abstract/intracranial-hemorrhage-with-direct-oral-anticoagulants-in-patients-with-brain-metastases/. Accessed September 9, 2020.