Anticoagulation in patients with brain cancer: an international registry

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON19911

Source
Nationaal Trial Register

Brief title
ABC Registry

Health condition

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.

Sponsors and support

Primary sponsor: Amsterdam UMC - location AMC
Source(s) of monetary or material Support: None

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

* Any ICH
* VTE and stroke or systemic atrial thromboembolism and
* In patients with an index ICH recurrent ICH during 90-days follow up post-ICH
* In patients with an index ICH functional status at 90-days post-ICH (Karnofsky Performance Status and FUNC score)

Study description

Background summary

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.

Study objective

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

Study design

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.

Intervention

N/A

Contacts

Public
Amsterdam University Medical Centers - location AMC
Eva Hamulyák

+31 20 5667516
Scientific
Amsterdam University Medical Centers - location AMC
Eva Hamulyák

+31 20 5667516

Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2015
Enrollment:	2200
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Ethics review

Positive opinion

Date:	23-10-2020
Application type:	First submission

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
NTR-new	NL8995
Other	METC AMC : W19_261 # 19.312

Study results

Summary results

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.