KURZPROTOKOLL
PRIDE-Studie

Öffentlicher Titel	Phase-IIa-Studie zur Radiochemotherapie unter Verwendung von Bevacizumab bei Patienten mit unbehandeltem MGMT-unmethylierten Glioblastom
Wissenschaftl. Titel	A phase IIa, open-label, multicenter study of radiochemotherapy with isotoxic dose escalation and protective VEGF inhibition using bevacizumab in the treatment of patients with first diagnosis of IDH wild-type, MGMT unmethylated glioblastoma
Kurztitel	PRIDE-Studie
Studienart	multizentrisch, prospektiv, offen/unverblindet, Register, Investigator Initiated Trial (IIT)
Studienphase	Phase II
Erkrankung	Nervensystem: Gliome: Glioblastom (WHO Grad IV) - Erstlinie
Einschlusskriterien	- 1.Diagnosis of glioblastoma, IDH-wildtype and MGMT unmethylated status must be proven histologically. MRI images must not be older than 2 weeks before initiating RT - 2. 18 and 70 years of age, smoking or non-smoking, of any ethnic origin - 3.Eastern Cooperative Oncology Group (ECOG) Performance Status 0–2 - 4.Patient must have provided signed informed consent (informed consent document to be approved by the institution's Independent Ethics Committee and consent obtained prior to any study-specific procedure). This includes the willingness to give written informed consent, written consent for data protection (according to the German General Data Protection Regulation (Datenschutz-Grundverordnung, DSGVO) in addition to willingness to participate and comply with the study - 5.Craniotomy or intracranial biopsy site must be adequately healed, free of drainage or cellulitis, and the underlying cranioplasty must appear intact at the time of inclusion - 6.Adequate hematological function: white blood cell (WBC) count  3x109/L, absolute neutrophil count (ANC) >1,5x109/L, platelet count 100x109/L, hemoglobin 8 g/dl (may be obtained by the use of erythropoietin-stimulating agents or transfusion for anemia) - 7.Adequate liver function: Total bilirubin < 1.5 x upper limit of normal (ULN) AND aspartate aminotransferase (AST), alanine aminotransferase (ALT) < 2.5 x ULN - 8.Adequate renal function: Serum creatinine 1.5 x ULN AND patients with urine dipstick for proteinuria < 2+ - 9.International normalized ratio (INR) (in absence of anticoagulation treatment) 1.5 within 7 days prior to enrolment. Anticoagulation is allowed if target INR is < 3 and if the patient is on a stable dose of anticoagulant (coumarin type, low molecular weight heparin (LMWH) or bivalirudin or argatroban) for >2 weeks at time of enrolment. Therefore, during the study, the preferred choice for anticoagulation treatment with therapeutic intent should be low molecular weight heparin as per ASCO guidelines - 10.Women of childbearing potential (i.e., a woman, who is biologically capable of becoming pregnant) must have a negative serum (-HCG) pregnancy test within 7 days prior to the first dose of study medication and radiotherapy; adequate contraception should be applied
Ausschlusskriterien	- 1. Positive test results for HbsAG, anti-HCV, anti-HIV-1/-2 - 2. Any other condition or treatment that, in the opinion of the Investigator, might interfere with the study or current drug - 3. Controlled substance abuse according to the German Narcotic Drugs Act (Betäubungsmittelgesetz, BtMG) - 4. Past medical history of diseases with poor prognosis according to the judgement of the investigator, e.g. severe coronary heart disease, severe diabetes, immune deficiency, residual deficits after stroke, severe mental retardation - 5. Foreseeable non-compliance with the protocol requirements, instructions and study-related restrictions, e.g. uncooperative attitude, inability to return for follow-up visits, and low probability of completing the study

- 6. Pregnancy or breast feeding
- 7. Patient is the investigator, research assistant, pharmacist, study coordinator, other staff or relative there of directly involved in the conduct of the study
- 8. Evidence of recent hemorrhage on postoperative MRI of the brain. However, patients with clinically asymptomatic presence of hemosiderin, resolving hemorrhagic changes related to surgery, and presence of punctate hemorrhage in the tumor are permitted entry into the study
- 9. Any prior radiotherapy to the brain or prior radiotherapy resulting in a potential overlap in the radiation field
- 10. Patients simultaneously enrolled in another clinical trial or patients who participated in another clinical trial during the 28 days (or five-half lives of the respective investigational product, whichever is longer) before enrolment
- 11.Patients who previously participated in this trial
- 12.Evidence for any active infection requiring hospitalization or i.v. antibiotics within 2 weeks prior to inclusion
- 13.Patients who are underage or patients who are incapable to understand the aim, importance and consequences of the study and to give legal informed consent (according to § 40 Abs. 4 and § 41 Abs. 2 und Abs. 3 AMG)
- 14.Patients who possibly are dependent on the sponsor or investigator
- 15.Immuno-compromised)patients, including known seropositivity for human immunodeficiency virus (HIV)
- 16.History of chronic gastrointestinal disease with diarrhea; history of abdominal or pelvic radiotherapy
- 17.Any other significant medical illness or medically significant laboratory finding that would, in the investigator’s judgement, make the patient inappropriate for this study, or would increase the risk associated with the patients’ participation in the study
- 18.Inability to undergo MRI
- 19.Contraindication and/or hypersensitivity to bevacizumab or its excipients. For details check the Summary of Product Characteristics of Aybintio®
- 20.Prior treatment with bevacizumab for any indication
- 21.Parallel administration of any drug suspected to interfere with bevacizumab at the time of inclusion
- 22.Significant cardiovascular disease defined as congestive heart failure (NYHA Class II, III, IV), unstable angina pectoris or myocardial infarction within 6 months prior to enrolment
- 23. Inadequately controlled hypertension (defined as a blood pressure of > 150 mmHg systolic and/or >100 mmHg diastolic on medication) or any prior history of hypertensive crisis or hypertensive encephalopathy
- 24. History of stroke or transient ischemic attack within 6 months prior to enrolment
- 25. Significant vascular disease (e.g., aortic aneurysm, aortic dissection or recent peripheral arterial thrombosis) within 6 months prior to enrolment
- 26.Evidence or history of recurrent thromboembolism (> 1 episode of deep venous thrombosis / peripheral embolism) during the past 2 years
- 27.Evidence of bleeding diathesis of coagulopathy (in the absence of therapeutic anticoagulation)
- 28.Chronic daily intake of aspirin > 325 mg/day or clopidogrel > 75 mg/day
- 29.History of intracranial abscess within 6 months prior to inclusion
- 30.History of abdominal or tracheoesophageal fistula, gastrointestinal perforation or intra-abdominal abscess within 6 months prior to study enrolment

	- 31.History of grade 2 hemoptysis according to NCI-CTC criteria within 1 month prior to inclusion - 32.Serious non-healing wound, ulcer or bone fracture - 33.Placement of a central vascular access device (CVAD) within 2 days prior to bevacizumab administration
Alter	18 - 64 Jahre
Molekularer Marker	MGMT Promoter, nicht methyliert
Sponsor	Deutsche Krebshilfe e.V.
Förderer	Deutsche Krebshilfe e.V.
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT05871021 EudraCT 2021-000565-32
Links	Weiterführende Informationen