KURZPROTOKOLL
Rosalie Studie

Öffentlicher Titel	Phase I/II Impfstudie zu EO2401 bei fortgeschrittenem Glioblastom
Wissenschaftl. Titel	A MulticenteR, Open-Label, First-in-Human, PhaSe Ib/IIa Trial of EO2401, a Novel Multipeptide Therapeutic VAccine, with and without PD-1 Check Point Inhibitor, FoLlowing Standard Treatment in PatIents with ProgrEssive Glioblastoma (Rosalie study)
Kurztitel	Rosalie Studie
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig
Studienphase	Phase I/II
Erkrankung	Nervensystem: Gliome: Glioblastom (WHO Grad IV) - Zweitlinie oder höher
Einschlusskriterien	- Patients with unequivocal documented (including histological confirmation of Glioblastoma-GB- at the primary diagnosis) evidence of progressive or first recurrent GB on MRI, as defined by RANO criteria - Patients with at least 1 measurable lesion - Patients with an age >= 18 years old - Patients who are human leukocyte antigen (HLA)-A2 positive - Patients with an Eastern Cooperative Oncology Group (ECOG) performance status <= 2 or Karnofsky performance status >= 70 - Patients should have received standard therapy, including surgery (biopsy, incomplete or complete resection), radiation, temozolomide, if applicable a. Radiation therapy must have been finished 28 days before first study treatment administration b. Patients who received temozolomide as adjuvant therapy must have stopped the treatment and have a wash-out period of 28 days before first study treatment administration (6 weeks for nitrosoureas and 5 half lives for experimental therapies) c. Patients with unmethylated methylguanine-DNA-methyltransferase (MGMT) promoter can be included even if they have not received temozolomide prior to the inclusion in this clinical study) - Female patients of childbearing potential must have a negative serum pregnancy test within 72 hours prior to dosing - Considering the embryofetal toxicity of the nivolumab shown on animals' models, the following recommendations for contraception must be followed: a. If not surgically sterile, female patients of childbearing potential age must use highly effective barrier contraception from signing the Informed Consent Form (ICF) through 6 months after the last treatment dose administered. Highly effective barrier and non barrier contraception included: i. Combined (estrogen and progesterone containing) hormonal contraception associated with inhibition of ovulation: Oral Intravaginal Transdermal ii. Progestogen-only hormonal contraception associated with inhibition of ovulation: Oral Injectable Implantable iii. Intrauterine device iv. Intrauterine hormone-releasing system v. Bilateral tubal occlusion vi. Sexual abstinence. In each case of delayed menstrual period (over 1 month between menstruations), confirmation of absence of pregnancy is strongly recommended. This recommendation also applies to women of childbearing potential with infrequent or irregular menstrual cycles. b. If not surgically sterile, male with female partner of childbearing potential must use condom from signing the ICF through 8 months after the last treatment dose administered. Males must ensure that their partners of childbearing potential use highly effective barrier contraception also - Patients having received the information sheet and who have provided written informed consent prior to any study-related procedures - Patients willing and able to comply with the scheduled visits, treatment plan, laboratory tests, and other study procedures indicated in the protocol

Ausschlusskriterien

- Patients treated with dexamethasone > 2 mg/day or equivalent (i.e., 13 mg/day of prednisone) within 14 days before the first EO2401 administration, unless required to treat an adverse event (AE) Note: The criterion is applicable at the time of screening and also at the time of study treatment start (i.e. the patient should not have received treatment with dexamethasone > 2 mg/day or equivalent in the time between screening and study treatment start; this should be checked at the time of treatment start)
- Patients treated with PD (L)-1(Programmed-cell Death/Programmed-cell Death Ligand) immunotherapy, radiotherapy, and cytoreductive therapy within 28 days before the first EO2401 administration
- Patients with tumors primarily located in the infra-tentorial segment
- Patients with known radiological evidence of extracranial metastases
- Patients with presence of new hemorrhage (excluding, stable Grade 1) or uncontrolled seizure
- Patients with significant leptomeningeal disease
- Patients with abnormal (>= Grade 2 National Cancer Institute-Common Terminology Criteria for AEs [NCI-CTCAE] version 5.0) laboratory values for hematology, liver, and renal function (serum creatinine). In detail, the following values apply as exclusion criteria: a. Hemoglobin < 10 g/dL (6.2 mmol/L) b. White blood cell count decrease (< 3.0 × 109/L) or increase (> 10.0 × 109/L) c. Absolute neutrophil count decrease (< 1.5 × 109/L) d. Platelet count decrease (< 75 × 109/L) e. Bilirubin > 1.5 × upper limit of normal (ULN; according to the performing laboratory's reference ranges) f. Alanine aminotransferase > 3 × ULN g. Aspartate aminotransferase > 3 × ULN h. Gamma-glutamyltransferase > 2.5 × ULN i. Serum creatinine increase (> 1.5 × ULN) j. Abnormal thyroid function: 0.3 > thyroid-stimulating hormone > 5 U(unit)/mL and 1.07 > free T3 > 3.37 nmol/L and 8.6 > free T4 > 25 pmol/L
- For patients who are planned to receive bevacizumab: Patients with nephrotic syndrome Patients with proteinuria >= 2g/24 hours Patients with history or active gastrointestinal perforation and fistula Significant surgical procedure in the 4 weeks preceding the start of treatment or planned surgery Unhealed wound Patient with recent (4 weeks) history of hemoptysis of ½ teaspoon or more of red blood Thrombotic episode within 6 months Uncontrolled diabetes mellitus or hypertension Posterior reversible encephalopathy syndrome
- Patients with persistent Grade 3 or 4 toxicities (according to NCI-CTCAE v5.0). Toxicities must be resolved since at least 2 weeks to Grade 1 or less. However, alopecia or other persisting toxicities Grade <= 2 not constituting a safety risk based on Investigator's judgment is acceptable
- Patients with contraindication to contrast-enhanced MRI
- Other malignancy or prior malignancy with a disease-free interval of less than 3 years except those treated with surgical intervention and an expected low likelihood of recurrence such as basal cell or squamous cell skin cancer, or carcinoma in situ. Patients with adequately treated basal cell or squamous cell skin cancer, or carcinoma in situ are eligible

- Patients with clinically significant cardiac disease, significant medical or psychiatric disease/condition that, in the opinion of the Investigator, would interfere with the evaluation of EO2401 or interpretation of patient safety or study results or that would prohibit the understanding or rendering of informed consent and compliance with the requirements of the protocol - including (but not limited to): New York Heart Association > Grade 2 congestive heart failure within 6 months prior to study entry Uncontrolled or significant cardiovascular disease, including: i. Myocardial infarction within 6 months prior to obtaining informed consent ii. Uncontrolled angina within 6 months prior to obtaining informed consent iii. Diagnosed or suspected congenital long QT syndrome iv. Any history of clinically significant ventricular arrhythmias (such as ventricular tachycardia, ventricular fibrillation, or Torsades de pointes) v. Unstable angina within 6 months prior to obtaining informed consent. c. Stroke within 6 months prior obtaining informed consent d. Concurrent neurodegenerative disease e. Dementia or significantly altered mental status
- Patients with suspected autoimmune or active autoimmune disorder or known history of an autoimmune neurologic condition (e.g., Guillain-Barré syndrome)
- Patients with vitiligo, type I diabetes mellitus, hypothyroidism due to autoimmune condition only requiring hormone replacement therapy, psoriasis not requiring systemic therapy, or conditions not expected to recur in the absence of an external trigger are permitted to enroll
- Patients with history of solid organ transplantation or hematopoietic stem cell transplantation
- Patients with history or known presence of tuberculosis
- Pregnant and breastfeeding patients
- Patients with history or presence of human immunodeficiency virus and/or hepatitis B virus/hepatitis C virus
- Patients who have received live or attenuated vaccine therapy used for prevention of infectious diseases including seasonal (influenza) vaccinations within 4 weeks of the first dose of study drug
- Patients with a history of hypersensitivity to any excipient present in the pharmaceutical form of investigational medicinal product
- Patients treated with herbal remedies with immunostimulating properties or known to potentially interfere with major organ function
- Patients with known drug and alcohol abuse
- Patients with known or underlying medical or psychiatric condition that, in the Investigator's opinion, would make the administration of study drug hazardous to the patient or obscure the interpretation of toxicity determination or AEs
- Patients who have received treatment with any other investigational agent, or participation in another clinical trial within 28 days prior to enrollment and during the treatment period
- Patients deprived of their liberty or under protective custody or guardianship

Alter 18 Jahre und älter

Status Aktiv

Prüfzentren

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Sponsor Enterome

Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT04116658 (primäres Register) EudraCT 2018-002279-16