A study of 2B3-101 in patients with solid tumors and brain metastases or recurrent malignant glioma.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26600

Source
NTR

Health condition

solid tumors, brain metastases

solide tumoren, hersenmetastasen
Recurrent Malignant Glioma

Sponsors and support

Primary sponsor: to-BBB Technologies B.V.
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Intervention

Outcome measures

Primary outcome

To assess the safety and tolerability of 2B3-101 in patients with solid tumors and brain metastases or recurrent malignant glioma, in order to determine the Maximum Tolerated Dose (MTD).

Secondary outcome

1. To examine the pharmacokinetics (PK) in plasma of 2B3-101 in terms of Cmax, Vss, T1/2, AUC, CL;

2. To obtain preliminary information on the clinical anti-tumor activity of 2B3-101 in terms of objective response rate and duration of response.

Study description

Background summary

This is a Phase I/IIa, multicenter, open-label, dose-escalation study. The study will be conducted in 2 stages: a Dose-Escalation Phase and an Expansion Phase. In the Dose-Escalation Phase, female and male patients with solid tumors and brain metastases will be enrolled. Patients will be assigned to a dose level cohort, each consisting of 3-6 patients. The starting dose of IV 2B3-101 infusions will be 5 mg/m2 followed by sequential cohorts with 2B3-101 doses of 10, 17, 25, 35, 47, and 62 mg/m2 etc, to be continued until a Dose-Limiting Toxicity (DLT) has been observed. The Maximum Tolerated Dose (MTD) is defined as the 2B3-101 dose level below the dose level at which at least two patients in a dose cohort experience a DLT.

In the Expansion Phase, only female patients with breast cancer and brain metastases or recurrent malignant glioma will be enrolled, and will be treated with IV infusions of 2B3-101 at the Maximum Tolerated Dose (MTD) as determined during the dose escalation part of the study.

For both the Escalation and Expansion Phase, each treatment cycle consists of 21 days. 2B3-101 will be administered IV on day 1 of each 21-day treatment cycle. Blood samples will be taken on day 1, 2, 3, 5, 8 and 11 in order to assess the PK profile during the first 2B3-101 treatment cycle.

A patient will stay on 2B3-101 treatment until disease progression, unacceptable toxicity, or discontinuation for any other reason.

Study objective

N/A

Study design

The MTD will be determined during the first 21 days after initial 2B3-101 administration.

PK blood samples will be taken during the first 11 days after initial 2B3-101 administration.

The preliminary anti-tumor activity of 2B3-101 will be measured every 6 weeks.

Intervention

The study will be conducted in 2 stages: A Dose-Escalation Phase and an Expansion Phase.

In the Dose-Escalation Phase, female and male patients with solid tumors and brain metastases or recurrent malignant glioma will treated with increasing doses of intravenously administered 2B3-101.

In the Expansion Phase, female patients with breast cancer and brain metastases will be treated with a single dose of intravenously administered 2B3-101.

Contacts

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Eligibility criteria

Inclusion criteria

1. Age at least 18 years;

2. Measurable or evaluable brain disease;

3. ECOG Performance Status ≤ 2;

4. Estimated life expectancy of at least 8 weeks;

5. Toxicities incurred as a result of previous anticancer therapy (radiation therapy, chemotherapy, or surgery) must be resolved to ≤ grade 2 (as defined by CTCAE version 4.0);

6. No evidence of (cortical) cognitive impairment as defined by a Mini-Mental Status Exam (MMSE) score ≥ 25/30;

7. No evidence of sub cortical cognitive impairment as defined by a score on HIV Dementia Scale (HDS) > 10;

8. Written informed consent according to local guidelines.

In addition to the above listed eligibility criteria, the following criteria are applicable:

9. Dose-Escalation Phase: Female and male patients with pathologically confirmed diagnosis of advanced, recurrent solid tumors and unequivocal evidence of brain metastases that are refractory to standard therapy or for which no standard therapy exists. Brain metastases may be stable, progressive, symptomatic or asymptomatic brain metastasis/es. Stable or decreasing dosage of steroids (e.g. dexamethason) for 7 days prior to baseline MRI or non-

enzyme inducing anti-epileptic drugs is allowed OR;

Female and male patients with pathology confirmed diagnosis of advanced, recurrent primary malignant (grade III and IV) glioma that are refractory to standard therapy or for which no standard therapy exists. Stable or decreasing dosage of steroids (e.g. dexamethason) for 7 days prior to baseline MRI or non-enzyme inducing anti-epileptic drugs are allowed;

10. Expansion Phase: Female patients with pathologically confirmed diagnosis of advanced, recurrent breast cancer with unequivocal evidence of brain metastases that are refractory to standard therapy or for which no standard therapy exist. Brain metastases may be stable, progressive, symptomatic or asymptomatic brain metastasis/es. Stable or decreasing dosage of steroids (e.g. dexamethason) for 7 days prior to baseline MRI or non-enzyme inducing anti-epileptic drugs is allowed.

Exclusion criteria

Prior Treatment:

1. Less than 4 weeks since the last treatment of chemotherapy, biological therapy, immunotherapy and systemic radiotherapy (except palliative radiation delivered to <20% of bone marrow), less than 8 weeks for cranial radiotherapy, and less than 6 weeks for nitrosoureas and mitomycin C;

2. Patients that have received a maximum cumulative dose of > 360mg/m2 for doxorubicin or > 600mg/m2 for epirubicin.

Current Treatment:

3. Current or recent (within 30 days of first study treatment) treatment with another investigational drug or participation in another investigational study.

Hematology, coagulation and biochemistry:

4. Inadequate bone marrow function: Absolute Neutrophil Count (ANC): < 1.5 x 109/L, or platelet count < 100 x 109/L or hemoglobin < 6 mmol/L;

5. Inadequate liver function, defined as:

A. Serum (total) bilirubin > 1.5 x the ULN for the institution if no liver metastases (> 2 x ULN in patients with liver metastases);

B. ASAT or ALAT > 2.5 x ULN if no liver metastases (> 4 x ULN in patients with liver metastases);

C. Alkaline phosphatase levels > 2.5 x ULN if no liver metastases (> 5 x ULN in patients with liver metastases, or > 10 x ULN in patients with bone metastases).

6. Inadequate renal function, defined as:

A. Serum creatinine > 1.5 x ULN.

Other:

7. Clinical suspicion or radiological evidence of leptomeningeal metastases;

8. Pregnancy or lactation. Serum pregnancy test to be performed within 7 days prior to study treatment start, or within 14 days followed by a confirmatory urine pregnancy test within 7 days prior to study treatment start;

9. For female subjects of childbearing potential (defined as < 2 years after last menstruation and not surgically sterile) and male subjects who are not surgically sterile or with female partners of childbearing potential: absence of effective, non-hormonal means of contraception (intrauterine contraceptive device, barrier method of contraception in conjunction with spermicidal gel);

10. Major surgical procedure (including open biopsy, excluding central line IV and portacath) within 28 days prior to the first study treatment, or anticipation of the need for major surgery during the course of the study treatment;

11. Grade 3 or 4 motor, sensory, or cranial neuropathy symptoms (as defined by CTCAE version 4.0);

12. Uncontrolled hypertension (systolic > 150 mm Hg and/or diastolic > 100mm Hg);

13. Clinically significant (i.e. active) cardiovascular disease defined as:

A. Stroke within ≤ 6 months prior to day 1;

B. Transient Ischemic Attack (TIA) within ≤ 6 months prior to day 1;

C. Myocardial infarction within ≤ 6 months prior to day 1;

D. Unstable angina;

E. New York Heart Association (NYHA) Grade II or greater Congestive Heart Failure (CHF);

F. Serious cardiac arrhythmia requiring medication;

G. Clinically relevant pathologic findings in ECG.

14. Left Ventricle Ejection Fraction (LVEF) by MUGA or ECHO < 50%;

15. Known hypersensitivity to any of the study drug components or excipients (e.g. doxorubicin, PEG or GSH);

16. Evidence of any other medical conditions (such as psychiatric illness, infectious diseases, physical examination or laboratory findings) that may interfere with the planned treatment, affect patient compliance or place the patient at high risk from treatment-related complications.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2011
Enrollment:	40
Type:	Anticipated

Ethics review

Positive opinion

Date:	06-09-2011
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	NL2913
NTR-old	NTR3059
Other	to-BBB technologies BV : 2B3-101-CR-001
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A