Randomized Open-label Phase II Study of CCNU versus CCNU + Dasatinib in Patients with Recurrent Glioblastoma.

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The general objectives are to assess the safety of combining dasatinib with CCNU as well as to assess activity of this combination and CCNU alone in GBM patients who have relapsed after prior treatment with temozolomide and radiotherapy

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON33494

Source
ToetsingOnline

Brief title
CCNU and Dasatinib in Glioblastoma, CA180-274.

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
braintumor, Recurrent gliobastoma

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharma Industry

Intervention

Keyword: CCNU, dasatinib, gliobastoma, Phase II

Outcome measures

Primary outcome

To estimate the proportion of subjects surviving without progression at 6 months (PFS-6) within the combination treatment arm (dasatinib plus CCNU).

Secondary outcome

1. Kaplan-Meier estimates of median PFS and PFS-6 (CCNU arm) and PFS-12.

2. Median overall survival and at 12 and 24 months.

3. Best overall response distribution, objective and complete response rates and median duration of objective or complete response.

4. Descriptive comparison of Time To Progression

5. Percentages of worst adverse events or Lab adverse events per AE term and category.

6. Correlation of angiogenesis and hypoxia markers expression and MGMT methylation status with clinical outcome.

Study description

Background summary

There is no *standard* nor widely-accepted treatment for patients with recurrent glioma. The median survival of patients with recurrent GBM is approximately 4 months, or approximately 6 months if a second resection is undertaken. Recurrent GBM therefore represents a clear unmet clinical need. There are very few agents which exert activity in GBM patients. Among these nitrosureas are probably the mostly widely used and lomustine (CCNU) falls under this class of cytotoxic agent. Because of the presence of a multitude of collateral upregulated signalling pathways in glioblastoma, the early

exploration of combination treatments are an attractive alternative scenario.

Study objective

The general objectives are to assess the safety of combining dasatinib with CCNU as well as to assess activity of this combination and CCNU alone in GBM patients who have relapsed after prior treatment with temozolomide and radiotherapy

Study design

The trial will integrate a non-randomised safety cohort aimed at documenting the safety profile and recommended dose of dasatinib in combination with CCNU, followed by a randomised Phase II study which will address the overall therapeutic strategy on combining dasatinib and CCNU or CCNU alone.

Intervention

Either Lomustine (oral) as a single therapy or Lomustine + Dasatinib (oral) as a combined therapy

Study burden and risks

Patients will be subject to invasive medical procedures (blood sampling, ECGs, MRIs, ECGs and chest X-Rays) but these procedures will be performed by trained medical staff so any risks or pain associated with these procedures should be minimised. The most commonly reported toxicities from either drug treatment is myelosuppression, nausea and vomiting as well as those as listed in the Informed consent form, some of which can be severe in nature. However, patients will be followed closely for toxicities and appropriate medical care given and based on previous human studies, these toxicities are manageable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Histologically- or cytologically-proven glioblastoma multiforme including anaplastic oligoastrocytoma with necrosis
2. Completion of Prior radiotherapy to brain > 3 months prior to the diagnosis of progression.
3. Recurrent disease documented by MRI scan within two weeks prior to start of study treatment.
4. No other chemotherapy regimens apart from Temozolomide are allowed. 5. Prior exposure in the adjuvant setting to biotherapies or a targeted agent is allowed if at least 4 weeks have elapsed since end of treatment and patients have recovered for all toxicities.
6. Patients may have been operated for recurrence. Surgery should be completed for at least 2 weeks before registration and patients should have fully recovered. An immediate (within 48hrs hours) MRI should be performed to document measurable residual disease
7. For non operated patients, recurrent disease must have at least one bidimensional target lesion of at least 2cm based on a MRI scan done within 2 weeks prior to registration.
10. Safety cohort only- Patients respiratory function (evaluated by DCLO) must be >60% of the predicted value.
11. Age >=18 years
12. WHO Performance status 0 - 2
13. Must be on a stable or decreasing dose of corticosteroids for at least 1 week prior to treatment start
14. Normal hematologic values
15. Normal liver function
16. Clinically normal cardiac function without history of ischemic heart disease in the past 12 months. Absence of cardiac insufficiency NYHA grade III and IV, instable angina & arrhythmia.

Exclusion criteria

1. No prior chemotherapy for recurrent disease.
2. No prior Gliadel wafers.
3. If any high-dose radiotherapy (> 65 Gy), stereotactic radiosurgery or internal radiation therapy has been performed, recurrence must be histologically confirmed.
4. No other malignancy [with exception of cone biopsied carcinoma of the cervix or treated basal or squamous cell skin carcinoma] in previous 3 years
5. All subjects (male and female) of reproductive potential must use effective contraception. Females must not be pregnant at entry or lactating.
6. Subjects should not be taking antiepileptic agents or be on non-enzyme-inducing antiepileptic drugs (non-EIAEDs).
7. No history of pulmonary disease that may affect pulmonary functions including obstructive chronic broncho-pneumopathy, concurrent pleural effusion and interstitial pneumonia.
8. No psychological, familial, sociological or geographical factors potentially hampering compliance with the study protocol and follow-up schedule

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2010
Enrollment:	18
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	CeCeNU®
Generic name:	lomustine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sprycel®
Generic name:	dasatinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	24-07-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-08-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-02-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-03-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-04-2010
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-07-2010

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2009-010576-21-NL
CCMO	NL28942.091.09
Other	volgt midden juli2009