



Fondation du Centre
Pluridisciplinaire d'Oncologie

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CHUV BH 06 - Rue du Bugnon 46 - 1011 Lausanne

ZOOM EORTC 26082-22081

Indication	Glioblastome, adjuvant
Title	Radiation therapy and concurrent plus adjuvant Temsirolimus (CCI-779) versus chemo-irradiation with temozolomide in newly diagnosed glioblastoma without methylation of the MGMT gene promoter – a randomized multicenter, open-label, Phase II study.
Protocol ID	EORTC 26082-22081
Phase	Phase II
Sponsor	EORTC (European Organisation for Research and Treatment of Cancer)
Local Principal Investigator	Dr R. Stupp
Primary Objective	The study's primary objective is to document the activity profile of CCI-779 by the evaluation of OS12 in patients with newly diagnosed glioblastoma (GBM) without methylation of the MGMT gene promoter, treated with CCI-779 before and concomitantly to RT, followed by CCI-779 maintenance therapy.
Inclusion/exclusion criteria	<p>Inclusion Criteria include the following :</p> <ul style="list-style-type: none"> ◆ Present with newly diagnosed histologically proven supratentorial GBM (World Health Organization (WHO) grade IV). The histological diagnosis can be obtained either from an open brain biopsy or from a neurosurgical resection of the tumor. ◆ Patients must be at least 18 years of age. ◆ Estimated life expectancy of at least 12 weeks. ◆ Tumor tissue specimens (paraffin-embedded and/or frozen) from the GBM surgery or open biopsy must be available for central pathology review, MGMT status determination and exploratory analysis of PI3-K/Akt/mTOR targets (P70S6K). ◆ A 25 ml EDTA blood sample is also required. ◆ WHO-ECOG Performance Status of ≤ 2. ◆ Clinically normal cardiac function without history of ischemic heart disease in the past 6 months and normal 12-lead electrocardiogram (ECG); no history of stroke. ◆ Absence of any psychological, familial, sociological or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial. ◆ Patients of childbearing/ reproductive potential should use highly

effective method of birth control as defined by the investigator. Women with childbearing potential must have a negative serum pregnancy test (β -HCG) \leq 14 days prior to registration and can not be breastfeeding.

◆ Before patient registration, written informed consent must be given according to ICH/GCP, and national/local regulations.

Exclusion Criteria include the following:

◆ Have had a prior malignancy within the last 5 years (other than adequately treated carcinoma in situ of the cervix, or non-melanoma skin cancer, with no subsequent evidence of recurrence).

◆ Having undergone only a stereotactic biopsy (open biopsy is allowed as ensuring sufficient tumor tissue yield).

◆ Unable to undergo Gd MRI.

◆ Have had chemotherapy within the last 5 years

◆ Prior chemotherapy for a brain tumor

◆ Prior RT of the head

◆ Are receiving concurrent administration of any other antitumor therapy

◆ Are using enzyme inducing anti convulsivants (in particular carbamazepine, phenobarbital and phenytoine) and are unable to discontinue use of these agents. Or any other strong inducers or inhibitors of CYP3A4.

◆ Planned surgery for other diseases (for example, dental extraction)

◆ Placement of Gliadel® wafer at surgery

◆ Have a serious concomitant systemic disorder (for example, active infection including HIV, or cardiac disease) that, in the opinion of the investigator, would compromise the patient's ability to adhere to the protocol. Patients with a QTc prolongation $>450/470$ msec (males/females) and patients who have a congenital long-QT-syndrome in their own or family medical history should be excluded, at the investigator's discretion.

◆ Known hypersensitivity to the study treatment

◆ Known hypersensitivity to antihistamines or other medical reason which prohibits the intake of antihistamines

◆ Current alcohol dependence or drug abuse

◆ Legal incapacity or limited legal capacity

◆ Have received treatment within the last 30 days with a drug that has not received regulatory approval for any indication at the time of registration