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**A PHASE III RANDOMIZED, PARALLEL GROUP, MULTI-CENTER STUDY IN RECURRENT GLIOBLASTOMA PATIENTS TO COMPARE THE EFFICACY OF CEDIRANIB ( RECENTIN, AZD2171 ) MONOTHERAPY AND THE COMBINATION OF CEDIRANIB WITH LOMUSTINE TO THE EFFICACY OF LOMUSTINE ALONE (IRB #13750)**

Glioblastoma is the most commonly occurring, malignant, central nervous system ( CNS ) tumor type, it grows rapidly, is highly invasive, and highly vascularized. Current treatment of glioblastoma is unsatisfactory. Median survival ranges from 9 - 15 months and less than 5% of subjects survive for 5 years. Most glioblastoma subjects undergo surgical resection, radiotherapy and chemotherapy. No standard treatment currently exists for recurrent glioblastoma and the prognosis for subjects with recurrent disease remains poor. The effective treatment of recurrent glioblastoma therefore represents an area of major unmet medical need.

Astra Zeneca has developed the small molecule tyrosine kinase inhibitor, Cediranib (RECENTIN, AZD2171), as a potent inhibitor for VEGF (vascular endothelial growth factor) signaling. In a disease setting where no standard of care exists, Cediranib may represent an important component for the future treatment of recurrent glioblastoma, the most serious and aggressive type of malignant brain tumor. VEGF and its receptor are known to be upregulated during malignant progression of glioma, and inhibition of VEGF signaling by Cediranib has the potential to halt the progression of the disease. The preliminary data from the ongoing study demonstrated biological activity in the recurrent glioblastoma setting.

This Phase III study is designed to compare the efficacy of Cediranib alone or in combination with oral lomustine to lomustine alone by assessment of progression free survival. Lomustine is one of the approved nitrosoureas being used in the treatment of recurrent glioblastoma.

Approximately 300 subjects with recurrent glioblastoma will be recruited in this and 10 subjects will be enrolled in CSMC. One hundred twenty subjects will be randomized to receive 30 mg of Cediranib in an open label monotherapy arm, 120 subjects will be randomized to receive 20 mg of Cediranib in combination with lomustine in a double blind combination arm, and 60 subjects will be randomized to receive lomustine in combination with Cediranib matched placebo in a double blind combination arm.

Each subject will come in for 11 visits ( including screening ). The study will involve physical exam, pulmonary function test, ECG, Labs, Urinalysis, Creatinine clearance, Neuro assessment, pregnancy test for women of child bearing potential, Dispensing of study medications, Collecting of concomitant medications and adverse events, Optional tumor sample for biomarker and pharmacogenetic analysis, Pharmacogenetic blood sample.

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