



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: December 24, 2008

To: Primary Clinical Research Associates

From: Janis Wobschall
Research Protocol Specialist

Re: N0776, Phase II Trial of Avastin® in Combination with Sorafenib in Recurrent Glioblastoma Multiforme

Immediately institute the following patient safety issue in accordance with your local IRB guidelines. An amendment to the study will follow in the next couple of weeks.

Eliminate intra patient dose escalation of Sorafenib, if \leq grade 2 toxicity in cycle 1. Rationale: Antitumor responses were seen in all patients who received the reduced Sorafenib dose of cycle 1 and had early MRIs performed. Cycle 1 in general has been well tolerated while all patients who received the higher Sorafenib dose in cycle 2 had toxicities, which necessitated dose omissions or delays. Therefore, intra patient Sorafenib dose escalation in cycle 2 appears to result in increased toxicity without necessarily improving efficacy; Sections 7 and 8 will be revised to eliminate the option of Sorafenib dose escalation.

If you have any questions, please feel free to contact me.