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To: All staff involved in the care and assessment of brain tumor patients – Mayo Clinic Rochester, Jacksonville, Scottsdale and University of Alabama at Birmingham

From: Paul D. Brown, MD and Kurt A. Jaeckle, MD (Study Chairs for protocol N0177)

Re: Protocol N0177: A phase I/II study of OSI-774 and temozolomide in combination with radiation therapy in glioblastoma multiforme.

Dear Colleagues:

With the recent report of the EORTC and NCIC study at this year's ASCO (Stupp R, et al: JCO, 2004 ASCO Annual Meeting Proceedings 22:1, 2004) revealing a significant survival advantage for temozolomide delivered concurrently and for 6 months after radiotherapy we felt it was imperative to modify our ongoing trial, N0177. The original trial (before addendum #6) was basically one week of daily OSI-774, followed by daily OSI-774 during radiotherapy, and after the radiotherapy was completed, daily OSI-774 was continued until tumor progression or excessive toxicity.

With recent amendments (#6 and #7) we have essentially added the "Stupp" regimen to the original N0177 trial. The trial will now be daily OSI-774 for 1 week, followed by daily OSI-774 and daily temozolomide during radiotherapy, and after the radiotherapy is completed, daily OSI-774 is continued until tumor progression or excessive toxicity. In addition approximately 1 month after the radiotherapy is completed 5 days of temozolomide will be given and this will be repeated every 28 days for a total of 6 cycles. These amendments have been approved by the NCI and we should be able to open up the phase I portions of the trial soon.

For those patients enrolled before addendum #6 (the "original" trial of only radiotherapy and OSI-774) we do not feel there are strong data to compel these patients to add temozolomide to their treatment regimens in the absence of progression. We would recommend the patients continue as they have been with their daily OSI-774 (same dose). If there are any toxicities, but a desire to continue with the OSI-774 at a lower dose, Section 8 of the protocol can still guide these dose reductions. If there is a desire to switch to or add temozolomide, this will have to be on an individual physician to patient basis, knowing if a patient does make the switch they will be going off study (and no longer taking OSI-774).

We are very excited about this change in protocol N0177, and if there are any questions please feel free to contact us.