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A Phase 2 Sensitivity and Selectivity Study of High-Dose 5-Aminolevulinic Acid in Adult Patients Undergoing Resection of a Newly Diagnosed or Recurrent Glioblastoma

Jeffrey W Cozzens [1], Barbara C Lokaitis [2], Kristin Delfino [2], Ava Hoeft [1], Brian E Moore [3], Amber S Fifer [2], Devin V Amin [1], José A Espinosa [1], Breck A Jones [1], Leslie Acakpo-Satchivi [1 4]

Affiliations
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Abstract

Background and objectives: The utility of oral 5-aminolevulinic acid (5-ALA)/protoporphyrin fluorescence for the resection of high-grade gliomas is well documented, but the problem of false-negative observations remains. This study compares high-grade glioma visualization with low/standard dose 5-ALA (<30 mg/kg) to high-dose 5-ALA (>40 mg/kg) to see if by using this higher dose, it is possible to reduce the rate of false-negative observations without increasing the rate of false-positive (FP) observations and therefore increase the sensitivity.

Methods: This is a prospective study of consecutive patients with radiological evidence of presumed high-grade glioma. We reviewed the data from patients who received preoperative low/standard doses and patients who received a preoperative high dose of 5-ALA. Adverse events, dose to observation time, intensity of tumor fluorescence, and results of biopsies in areas of tumor and tumor bed under deep blue light were recorded.

Results: A total of 22 patients with high-grade glioma received a dose >40 mg/kg (high-dose) and 9 patients received <30 mg/kg (low/standard dose). There were no serious adverse events related to 5-ALA in any subject. There was a very high sensitivity and specificity of 5-ALA for the presence of tumor in both groups. There were no FP observations (fluorescence with no tumor) in either group. The specificity and the positive predictive value were 100% in both groups. The sensitivity and the negative predictive value were 53.3% and 30.0% in the low/standard dose group and 59.5% and 31.8% in the high-dose group, respectively.

Conclusion: High-dose oral 5-aminolevulinic/protoporphyrin fluorescence is a safe and effective aid to the intraoperative detection of high-grade gliomas with high sensitivity and specificity. False-negative observations with a high dose do not seem to be less than that with a low/standard dose. The rate of FP observations with both groups remains very low.

Trial registration: ClinicalTrials.gov NCT01128218.