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Use of 5-ALA fluorescence-guided surgery versus white-light conventional microsurgery for the resection of newly diagnosed glioblastomas (RESECT study): a French multicenter randomized phase III study

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Abstract

Objective: Only one phase III prospective randomized study, published in 2006, has assessed the performance of 5-aminolevulinic acid (5-ALA) fluorescence-guided surgery (FGS) for glioblastoma resection. The aim of the RESECT study was to compare the onco-functional results associated with 5-ALA fluorescence and with white-light conventional microsurgery in patients with glioblastoma managed according to the current standards of care.

Methods: This was a phase III prospective randomized single-blinded study, involving 21 French neurosurgical centers, comparing 5-ALA FGS with white-light conventional microsurgery in patients with glioblastoma managed according to the current standards of care, including neuronavigation use and postoperative radiochemotherapy. Randomization was performed in a 1:1 ratio stratified by institution. 5-ALA (20 mg/kg) or placebo (ascorbic acid) was administered orally 3-5 hours before the incision. The primary endpoint was the rate of gross-total resection (GTR) blindly assessed by an independent committee. Patients without a confirmed pathological diagnosis of glioblastoma or with unavailable postoperative MRI studies were excluded from the per-protocol analysis.

Results: Between March 2013 and August 2016, a total of 171 patients were assigned to the 5-ALA fluorescence group (n = 88) or to the placebo group (n = 83). Twenty-four cases were excluded because the WHO histological criteria of grade 4 glioma were not met. The proportion of GTR was significantly higher in the 5-ALA fluorescence group (53/67, 79.1%) than in the placebo group (33/69, 47.8%; p = 0.0002). After adjustment for age, preoperative Karnofsky Performance Scale score, and tumor location, GTR was still associated with 5-ALA fluorescence (OR 4.13 [95% CI 1.94-8.79]). The mean 7-day postoperative Karnofsky Performance Scale score (≥ 80% in 49/71, 69.0% [5-ALA group]; 50/71, 70.4% [placebo group], p = 0.86) and the proportion of patients with a worsened neurological status 3 months postoperatively (9/68, 13.2% [5-ALA group]; 9/70, 12.9% [placebo group], p = 0.95) were similar between groups. Adverse events related to 5-ALA intake were rare and consisted of photosensitization in 4/87 (4.6%) patients and hepatic cytolysis in 1/87 (1.1%) patients. The 6-month PFS (70.2% [95% CI 57.7%-79.6%] and 68.4% [95% CI 55.7%-78.1%]; p = 0.39) and 24-month OS (30.1% [95% CI 18.9%-42.0%] and 37.7% [95% CI 25.8%-49.5%]; p = 0.89) did not significantly differ. In multivariate analysis, GTR was an independent predictor of PFS (hazard ratio 0.56 [95% CI 0.36-0.86], p = 0.008) and OS (hazard ratio 0.65 [95% CI 0.42-1.01], p = 0.05). The use of 5-ALA FGS generates a significant extra cost of 2732.36€ (95% CI 1658.40€-3794.11€).

Conclusions: The authors found that 5-ALA FGS is an easy-to-use, cost-effective, and minimally time-

consuming technique that safely optimizes the extent of resection in patients harboring glioblastoma amenable to a large resection.

Keywords: 5-ALA; extent of resection; fluorescence-guided surgery; glioblastoma; oncology; randomized study; tumor.