# Randomized, Multi-Center Phase 3 Trial of Pafolacianine during Intraoperative Molecular Imaging of Cancer in the Lung: Results of the ELUCIDATE Trial

Objective: To confirm the efficacy of Intraoperative Molecular Imaging (IMI) utilizing a targeted optical imaging agent (pafolacianine) to visually localize lung nodules, identify occult tumors and assess specimen tumor margins during a standard pulmonary resection.

Methods: Patients with suspected or biopsy-confirmed cancer in the lung scheduled for sublobar resection were administered a single intravenous infusion of pafolacianine (0.025 mg/kg), 1-24 hours prior to surgery. Intraoperatively, the patients underwent a white light evaluation, and, then, were randomly assigned to IMI or not (10:1). The primary study endpoint was the proportion of patients with a clinically significant event (CSE) which was defined as an unexpected event attributed to IMI with pafolacianine detecting cancer that would have been otherwise missed by standard surgical practice. Study CSEs were counted in three possibilities: IMI with pafolacianine (i) localized the index lung nodule that could not be located by white light, (ii) identified a synchronous malignant lesion, or (iii) identified a close surgical margin (<= 10mm).

Results: 112 patients were confirmed as eligible and administered pafolacianine. Of those receiving study drug, 111/112 proceeded to surgery and randomization; 1 patient withdrew consent prior to surgery. 100 patients were randomized to white light and IMI; 11?patients were assigned to white light only. Of the 100 patients randomized to IMI with pafolacianine, 54 patients (54%, 95% CI 43.7 – 64.0, $p < 0.0001$) had one or more CSEs. IMI with pafolacianine located the index lesion in 19 patients (19%, 95% CI 11.8 – 28.1) whose tumor could not be seen by white light. Also, IMI with pafolacianine identified occult synchronous malignant lesions in 9 patients (9%, 95% CI 4.2 – 16.4). Most (73%) IMI-identified synchronous malignant lesions were outside the planned field of resection. IMI with pafolacianine found 38 patients with close margins <=10 mm (38%, 95% CI 28.5 – 48.3). The investigators indicated a change in scope in the surgical procedure based on IMI with pafolacianine for 29% (22% increase, 7% decrease) of the patients. In the group randomized to IMI pafolacianine, there were 8/78 (10%) NSCLC patients whose stage was changed due to the CSE. No drug-related serious adverse events occurred. Pafolacianine infusion reactions, characterized primarily by mild gastrointestinal complaints, were seen in 19/112 (17%), of which 11 (10%) resulted in interruption of the infusion with eventual completion (6) or discontinuation (5).

Conclusions: Pafolacianine represents a first-in-class targeted imaging agent to aid the surgeon during surgery to visualize otherwise undetected cancers in the lung. In this trial, CSEs attributed to pafolacianine IMI occurred in more than 50% of patients undergoing surgery for pulmonary nodules. These findings suggest the use of IMI with pafolacianine may be a significant potential advancement to use during standard-of-care lung cancer surgery.

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