

MSOR5 Presentation Time: 5:20 PM**5-aminolevulinic Acid (5-ALA) Use with Concurrent Intraoperative Radiotherapy: Interim Analysis of the INTRAGO II Trial for Glioblastoma**

Christopher P. Cifarelli, MD, PhD, MMM¹,
 Kevin Petrecca, MD², Henning Kahl, MD³,
 Oliver Ganslandt, MD, PhD⁴, Tamer Abdelrhman, MD, PhD⁵,
 Stephanie Combs, MD⁶, Gustavo Sarria, MD⁷,
 Frank A. Giordano, MD⁸

¹West Virginia University, Neurosurgery & Radiation Oncology, Morgantown, WV, USA; ²McGill University, Neurosurgery, Montréal, QC, Canada; ³University Hospital Augsburg, Radiation Oncology, Augsburg, Germany; ⁴University Hospital Stuttgart, Neurosurgery, Stuttgart, Germany; ⁵Loyola University, Radiation Oncology, Chicago, IL, USA; ⁶University Hospital Munich, Radiation Oncology, Munich, Germany; ⁷University Hospital Bonn, Radiation Oncology, Bonn, Germany; ⁸University Hospital Mannheim, Radiation Oncology, Mannheim, Germany

Purpose: While the use of 5-ALA has been used to increase the extent of surgical resection in glioblastoma (GBM), its potential to act as a radiosensitizer has not been widely studied in the CNS. Whereas typical external beam radiotherapy (EBRT) treatments occur weeks after surgery and 5-ALA administration, intraoperative radiotherapy (IORT) delivers radiation while protoporphyrin IX is still present in residual tumor. This current study examines the potential for radiation necrosis (RN) development following IORT and subsequent fractionated radiotherapy.

Methods: Interim data from the INTRAGO II study for newly diagnosed GBM (NCT02685605) were analyzed for the incidence of radiation necrosis (RN) based on 5-ALA use, IORT treatment vs SOC control (60Gy EBRT), and extent of resection. Statistical analysis was performed via univariate (ANOVA), multivariate (Cox regression), and K-M estimations with significance of $p < 0.05$.

Results: 234 patients were enrolled in INTRAGO II between 2016 and 2022. Of these, 185 (79%) had a surgical resection performed with the use of 5-ALA tumor fluorescence visualization. Following surgical resection with 5-ALA, 94 (51%) received IORT (30Gy to the margin) and an additional 60Gy EBRT (ARM A). Imaging confirmed RN occurred in 11 (12%) of ARM A patients who had 5-ALA assisted resection, compared to 3 (3.3%) of ARM B patients who received only 60Gy EBRT. In the 49 patients not receiving 5-ALA, the imaging confirmed the RN rate in ARM A patients was 21% (5/24) compared to 12% in ARM B (3/25). The median time to development of RN was 236 days post-IORT and 158 days post completion of EBRT. ANOVA demonstrated a significantly ($p = 0.025$) higher rate of RN in ARM A patients overall, but not with the addition of 5-ALA. Cox regression analysis confirmed that only significant predictor of RN on multivariate analysis was IORT plus EBRT ($p = 0.033$) and KM estimations-Log Rank test of RN incidence were greater in Arm A/IORT patients than SOC/Arm B ($p = 0.029$).

Conclusions: While patients receiving IORT at the time of surgical resection had a higher rate of RN after SOC 60Gy EBRT, the use of 5-ALA in conjunction with surgical resection did not increase RN incidence. Further analysis will need to consider local PFS rates and the impact of 5-ALA use with IORT.

