

Feasibility of Combining Capecitabine and Temozolomide with yttrium 90 Radioembolization (CapTemY90) for Intermediate-Grade Metastatic Neuroendocrine Tumors

Michael C. Soulen MD¹; Ursina Teitelbaum MD¹; David Metz MD¹; Jeffrey I Mondschein MD¹; Bruce Giantonio MD¹; S. William Stavropoulos MD¹; Tracy Evans MD¹; Nevena Damjanov MD¹

¹Divisions of Interventional Radiology, GI Medical Oncology, and Gastroenterology, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA

Purpose: Grade 2 neuroendocrine tumors (NET) have an intermediate proliferative rate and progress more aggressively than low-grade NETs. The combination of capecitabine and temozolomide (CapTem) has been shown to achieve response rates of 61% in well-differentiated NETs. Capecitabine is synergistic with radiation and often used concurrently in other malignancies. We investigated the safety and tolerability of combining CapTem with Y90 radioembolization for progressive Grade 2 NETs with liver-dominant metastases.

Methods: Patients were treated with capecitabine 600 mg/m² twice daily for 14 days and temozolomide 150-200 mg/m² in two divided doses on Days 10-14, with 14 days between cycles. Simulation angiography and MAA scan for Y90 planning were performed during the first cycle of chemotherapy. During the second cycle, Y90 radioembolization with resin microspheres was performed to one lobe on Day 7. The other lobe was treated if needed on Day 7 of the 3rd or 4th cycle. CapTem was continued monthly. Clinical and laboratory toxicities were assessed monthly. Imaging was performed 3 months after the first radioembolization, then every 3 months. This retrospective analysis was IRB approved.

Results: 14 patients were treated. Primary NETs were pancreatic (6), bronchial (3), small bowel (3), and rectal (2). 12/14 patients completed the prescribed combination of oral chemotherapy and radioembolization. One heavily pre-treated patient developed Grade 2 hyperbilirubinemia after the first radioembolization and did not have the other lobe treated. One had severe post-embolization syndrome after the first radioembolization and declined the second one. 10/14 patients stopped CapTem at 3-31 months due to toxicity or progression, the other 4 remain on CapTem for 2 months – 4 years. As expected, G1-G2 fatigue, nausea, or thrombocytopenia was observed in most patients. Three patients had G3 toxicities, one each thrombocytopenia, fatigue, and pain. Mean decrease in CgA was 80%. One patient progressed in the liver at 21 months, the remainder are free from intrahepatic progression at 6-25 months. Three patients died, two from extrahepatic progression (7, 32 months) and one from REILD (17 months).

Conclusion: CapTemY90 is a tolerable regimen with toxicities similar to those reported for CapTem or Y90 alone. Responses are encouraging and supports further evaluation in a multicenter Phase 2 trial.