Safety & feasibility of integrated capecitabine and temozolomide with yttrium 90 radioembolization (CapTemY90) for WHO Grade 2 neuroendocrine tumors

Michael C. Soulen MD FSIR FCIRSE, Diana van Houten CRNP, Ginna Deitrick CRNP, Mandeep Dagli MD,
Jeffrey I. Mondschein MD FSIR, Ursina Teitelbaum MD, Nevena Damjanov MD, Mark O'Hara MD, Keith Cengel MD, David Metz MD
Neuroendocrine Tumor Program, Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA

BACKGROUND

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 this population. Capecitabine is synergistic with radiation and often used concurrently in other malignancies. We investigated the safety and tolerability of combining CapTem with Y90 radioembolization (TARE) for progressive Grade 2 NETs with liver-dominant metastases.

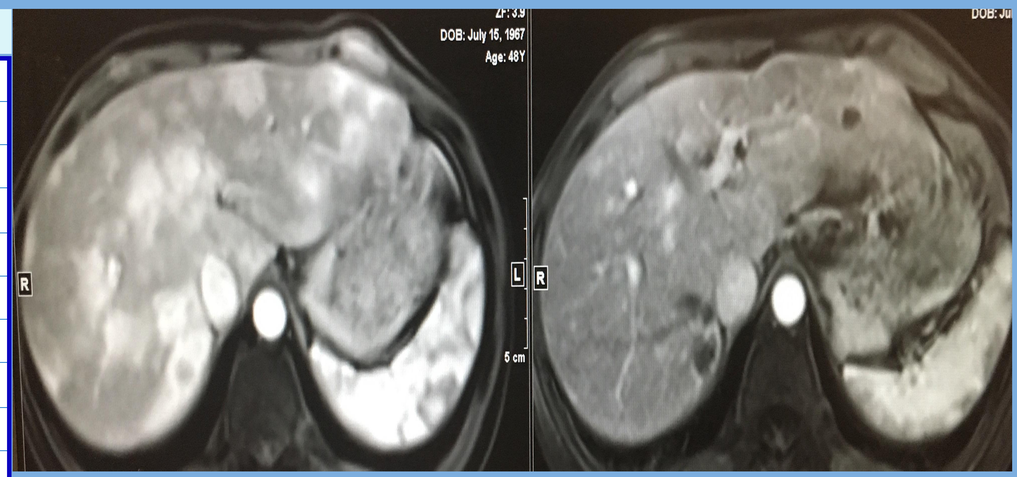
METHODS

- Patients with liver dominant G2 NET 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 TARE planning were performed during the first cycle of chemotherapy.
- During the second cycle, TARE 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 every 3 months after TARE.

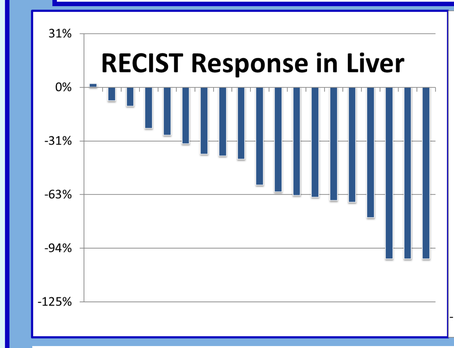
RESULTS

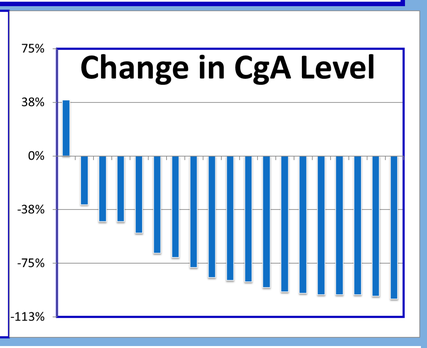
PATIENTS	N=21
Gender	13M/8F
Age (mean, range)	58 (35-76)
PRIMARY TUMOR	
Pancreas	8 (38%)
GI	7 (33%)
Bronchial	4 (19%)
PRIOR THERAPIES	
Octreotide	20 (95%)
Liver-directed (resection/embo/ablation)	4 (19%)
Primary resected	10 (48%)
Cytotoxic chemotherapy	2 (9.5%)
Evirolimus	5 (24%)

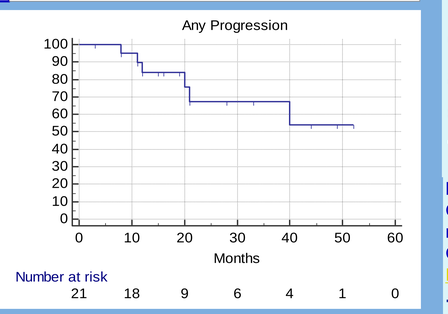
TOXICITIES	G1	G2	G3	G4
FATIGUE	9	2	1	
THROMBOCYTOPENIA	5		3	3
BILIRUBIN		2		
NAUSEA	7		1	
HFSR	1	2	1	



Arterial-phase enhanced MRI before and 1-year after CapTemY90, showing complete resolution of enhancing liver metastases.







- A total of 236 cycles of CapTem were administered, median 8 per patient (mean 11, range 4-32). 9 patients had dose reduction or interruptions for cytopenias (5), fatigue (4), nausea (3), and/or hand-foot skin reaction (2). CapTem was finally stopped due to chronic clinical toxicity (fatigue/nausea) in 8 patients, thrombocytopenia in 5, elevated liver function tests in 3, hand-foot skin reaction in 3, tumor progression in 3, and sustained response beyond two years in 2, with 3 patients having more than one indicator.
- 19/21 patients completed the prescribed TARE protocol; 2 did not get the second lobe treated due to post-embolization toxicities.
- Toxicities were as expected for CapTem and Y90 individually.
- ORR in the liver was 74%, including 3 CR, 11 PR, 5 SD, 2 unevaluable.
- ORR outside the liver was 55% including 6 PR and 5 SD among 11 evaluable patients.
- Median reduction in CgA was 87%, with 16/20 achieving >50% reduction.
- At median f/u of 22 mo (10-52 mo), median TTP was not reached. Mean TTP was 38.5 mo [30-47 mo] and mean TTHP was 42.5 mo [34-51 mo].

CONCLUSIONS

CapTemY90 is a feasible and tolerable regimen with additive toxicities. Response rate and duration are encouraging and support further evaluation in a Phase 2 trial.

REFERENCES
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