



Integrating Yttrium-90 Radioembolization with Capecitabine-Temozolomide for Grade 3 Liver-Dominant Metastatic Neuroendocrine Tumors: Initial Outcomes

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BACKGROUND

- Well-differentiated Grade 3 Neuroendocrine Tumors (NETs) are characterized by a Ki67 > 20% and greater than 20 mitoses/high power field
- G3 NETs have worse PFS and OS following embolotherapy (chemoembolization, radioembolization, or bland embolization)¹
- Capecitabine-temozolomide are radiosensitizers and have shown synergy when combined with TARE for G2 NETs²

FIGURE 1: HPFS and OS after LDT by Tumor Grade

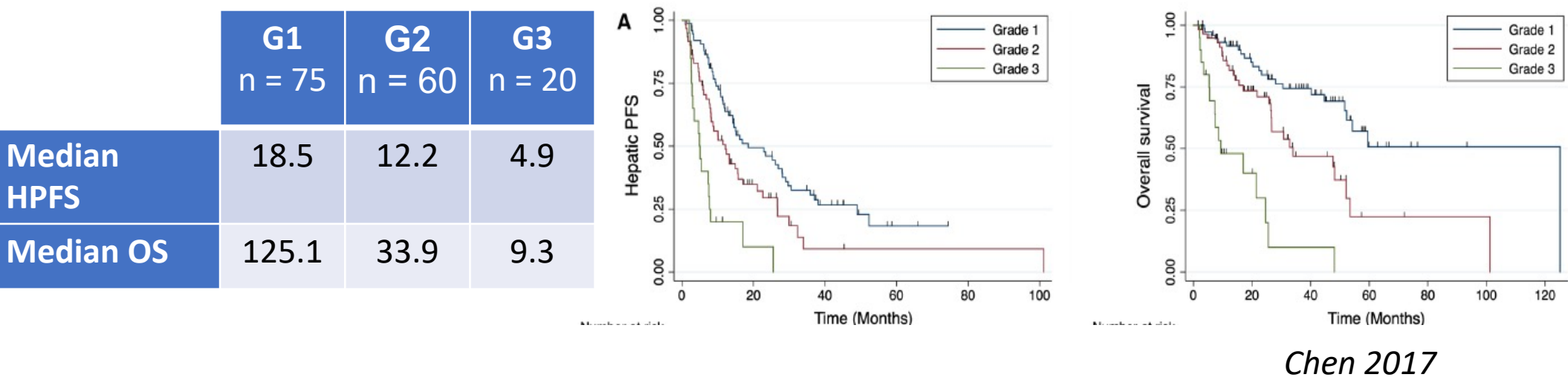
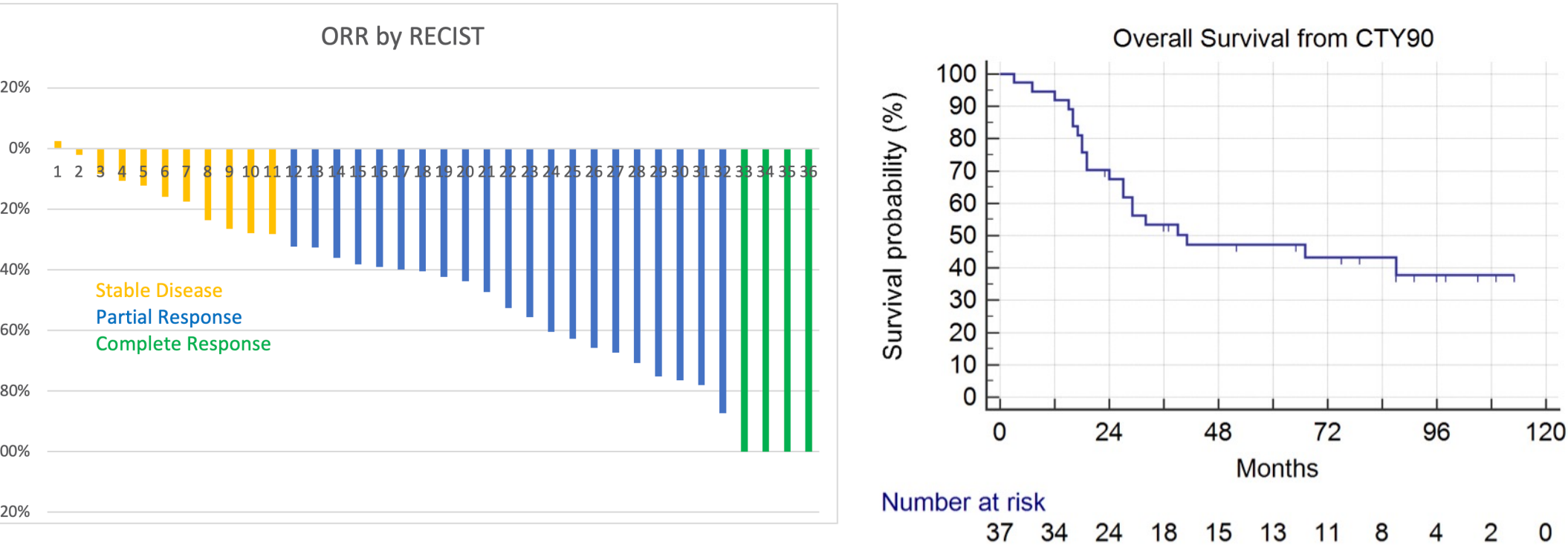


FIGURE 2: ORR and OS of G2 NETs after CapTemY90



METHODS

Capecitabine-Temozolomide-Y90 Regimen (CapTemY90)

- Capecitabine- temozolomide**
Capecitabine 750 mg/m² twice daily for 14 days
Temozolomide 200 mg/m² in two divided doses day 10-14
14 days between cycles
- Y90 Radioembolization**
Mapping during first cycle of CapTem
Dominant lobe treated on Day 7 of Cycle 2 of CapTem
BSA dosimetry
If bilobar metastases, other lobe treated on Day 7 of C3 or C4
- CapTem continued until progression or intolerance

Inclusion Criteria: Unresectable Grade 3 NET liver-dominant metastases without contraindication to TARE or CapTem
Liver dominance: > 50% total body tumor burden confined to liver
Liver tumor burden < 75%, patent portal vein
Preserved liver function, TBili <2 mg/dL
Cr < 2 mg/dL, Pt >100,000/cL

RESULTS

Patient Characteristics

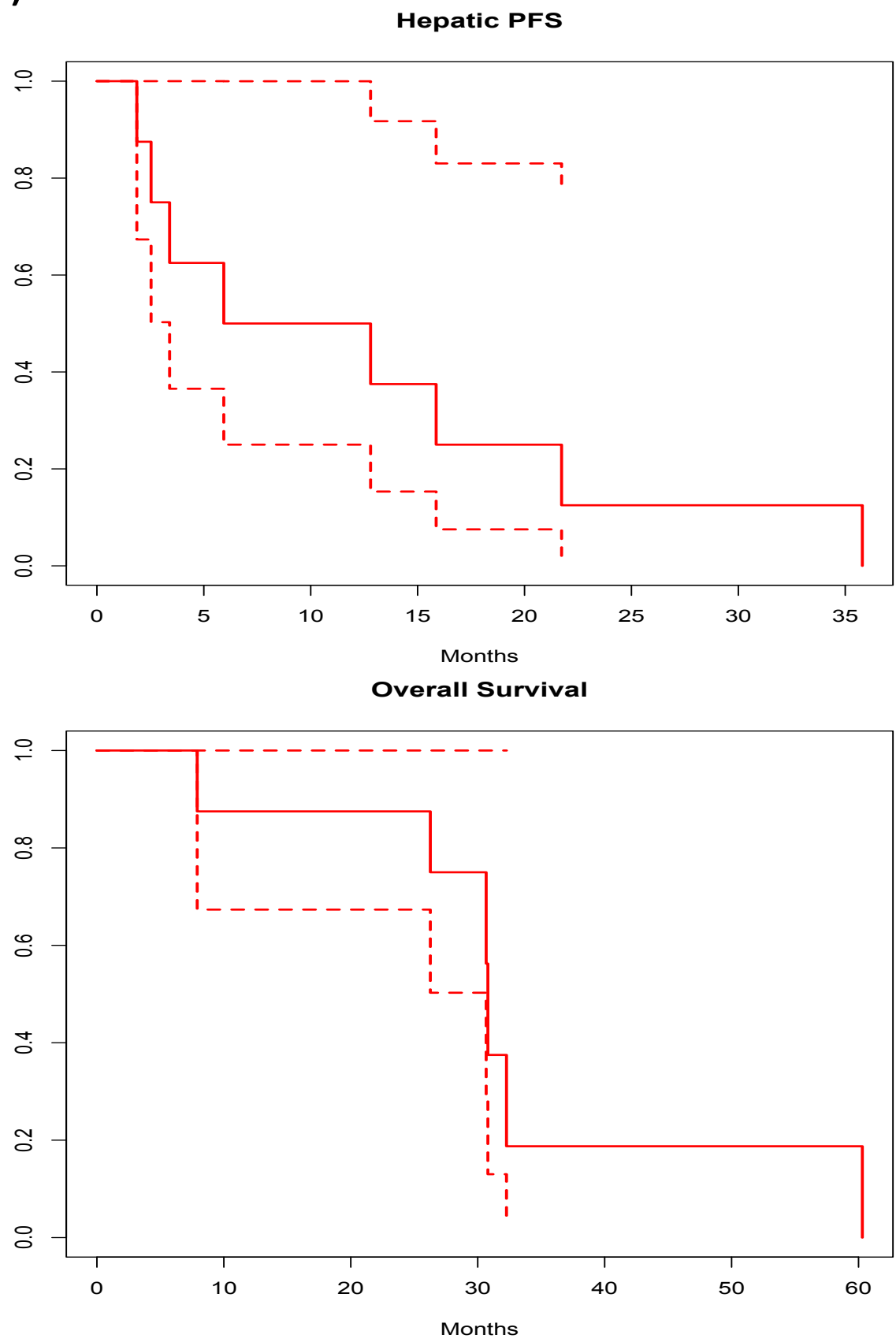
N = 8 patients	
PATIENT CHARACTERISTICS	n (%)
Age, median (range)	59 (46-73)
Sex, male	6 (75)
ECOG performance status 0-1	6 (75)
Site of primary tumor	
Pancreas	7 (88)
Lung	1 (13)
Primary resected	2 (25)
Bilobar liver metastases	8 (100)
Liver tumor burden	
<25%	2 (25)
25-50%	5 (63)
>50%	1 (13)
Extrahepatic metastases	2 (25)
Months from primary Dx, median (range)	11 (1-27)
Prior therapy	
SSA	6 (75)
Targeted agents (everolimus, sunitinib)	1 (13)
Cytotoxic chemotherapy	3 (38)
PRRT	1 (13)
Embolotherapy	1 (13)
Ki67 index, median (range)	37 (21-70)
Baseline CgA, median (range)	199 (90-6496)

Treatment Characteristics

- Duration CapTem, *median* = 9 months, (range 4-16 months)
- Months from Dx of liver metastases to first Y90, *median* = 15, (range 1-71mo)
- N = 13 radioembolizations
 - Median dose per patient: 48 mCi (range 33 – 66 mCi)

Outcomes

By RECIST 1.1, there were 4 PR, 2 SD, 2 PD, ORR = 50%
Median follow up 32 months (range 8 – 59 mo)



Outcome	Median (range)
Median hepatic PFS:	9.3 months (2.8 - 40.5 mo)
Median extrahepatic PFS:	16.4 months (7.1 – 28.3 mo)
Median overall survival:	30.8 months 6 deaths between 8 – 60 months

RESULTS: Toxicities

Common Terminology Criteria for Adverse Events 4.0

CTC Grade	1	2	3	4	5
Nausea	2				
Fatigue	6				
Pain	4				
Edema	1				
Hand-foot Skin Reaction	1				
Anorexia		1			
CKD	1				
ALT/AST			2*		
Hyperbilirubinemia			1		
Anemia			1		
Thrombocytopenia	1			1*	

*led to temporary hold and dose reduction

Three patients were treated with subsequent therapies upon progression:

- 1 patient with everolimus and sunitinib
- 1 patient with CapTem and proton therapy
- 1 patient with immunotherapy (nivolumab + ipilimumab)

DISCUSSION

- Integrated CapTem Y90 regimen showed acceptable toxicities in G3 patients, not more than additive
- Though this is a small cohort, initial outcomes appear improved compared to reported outcomes of embolotherapy alone with HPFS of 9.3 months versus 4.9 mo and OS of 30.8 months versus 9.3 months

REFERENCES

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