Randomized Embolization Trial for Neuroendocrine Tumor Liver Metastases (RETNET), NCT02724540

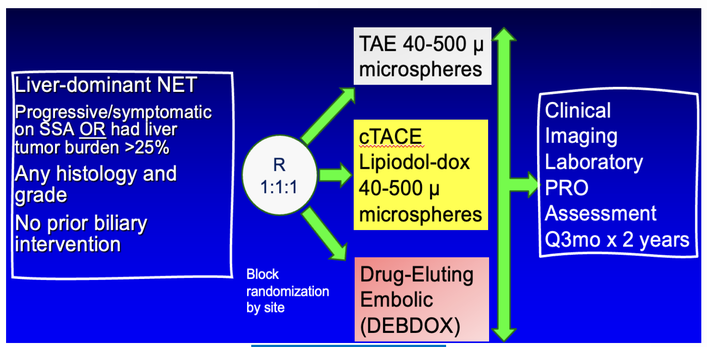
Michael Soulen MD[1], Nicholas Fidelman MD[2], Ricardo Garcia Monaco MD PhD[3], Ghassan El-Haddad MD PhD[4], Chris Dey MD[5], Rony Avritscher MD PhD[6], Nishita Kothary MD[7], Khashayar Farsad MD PhD[8], Sarah White MD MSc[9], Francesco DeCobelli MD PhD[10], Etay Ziv MD PhD[11], Robert Lewandowski MD[12]
[1]University of Pennsylvania, [2]UCSF, [3]Hospital Italiano, [4]Moffitt Cancer Center, [5]Sunnybrook Health Sciences Center, [6]MDACC, [7]Stanford, [8]OHSU, [9]Medical College of Wisconsin, [10]Hospital San Rafaelle, [11]MSKCC, [12]Northwestern

Background

Embolotherapy is recommended in international guidelines for treatment of progressive or symptomatic neuroendocrine tumor (NET) liver metastases. Different embolotherapy techniques are used without strong evidence regarding relative efficacy, safety, and patient experience.

Methods

- International multicenter open-label trial of patients with NET liver metastases randomized to conventional transarterial chemoembolization (TACE), transarterial embolization (TAE), or DEBDOX.
- Primary endpoint hepatic progression-free survival (HPFS) by blinded central read.
- Safety assessments at 10 and 30 subjects per arm then annually with a stopping rule of 20% TR-SAE rate.



SCHEMA

Results

The DEE arm was closed due to a TR-SAE rate of 40%.
151 patients randomized to TAE vs. cTACE, well matched for all variables.

	TAE N=78	cTACE N=73	P value
Age, mean(SD)	61.1(12.9)	62.8(9.8)	0.37
Race, W/B/O (%)	78/8/14%	81/8/11%	0.44
Histology			0.82
gut	41 (53%)	41 (56%)	
pancreas	29 (37%)	25 (34%)	
lung	4 (5%)	2 (3%)	
other	4 (5%)	5 (7%)	
Grade 1/2/3 (%)	37/56/1%	36/56/5%	0.46
Extrahep mets	46 (59%)	41 (56%)	0.73

	TAE N=78	cTACE N=73	P value
Liver Burden			0.80
<25%	40 (51%)	35 (48%)	
25-50%	29 (37%)	27 (37%)	
>50%	9 (12%)	11 (15%)	
ECOG 0/1/2 (%)	71/27/3%	51/19/4%	0.87
Symptom Score, mean(SD)	1.5 (0.7)	1.6 (0.9)	0.49
Indication: Symptoms	35 (45%)	32 (44%)	0.90
Progression	54 (69%)	58 (79%)	0.15
Tumor Burden	38 (49%)	37 (51%)	0.81

TR-SAE PER INVESTIGATOR ASSESSMENT

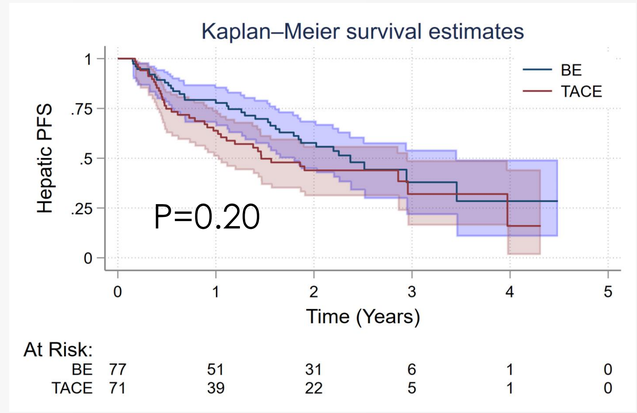
	TAE N=78			TACE N=73		
	Grade 3-4	SIR D-E	both	Grade 3-4	SIR D-E	both
Pain	3	2	1	6	6	5
Hypertension	10	4	4	2	1	1
Delerium	2	3	0			
Liver Failure	2	2	2			
hyponatremia	2	1	1	1	0	0
hypokalemia	1	0	0	1	0	0
Hyperglycemia	1	1	1			
hypoxia	0	1	0	1	0	0
infection	1	1	1			
anaphylaxis	1	0	0			
Cholecystitis	1	0	0			
tachycardia	0	1	0			
fever	0	1	0			
hiccups	1	1	1			
weakness	1	1	1			
PES	1	0	0			
AKI				2	2	1
transaminitis				3	0	0
seizure				0	1	0
vomiting				0	1	0
headache				1	1	1
	27 (35%)	19 (24%)	12 (15%)	17 (23%)	12 (16%)	8 (11%)

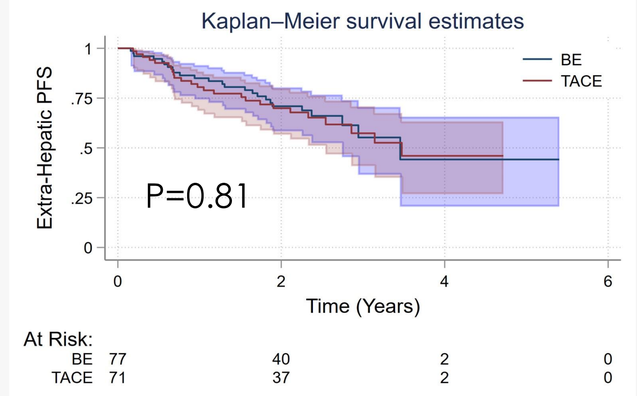
Serious Adverse Events by CTCAE and/or SIR criteria were 50% higher with TAE

Conclusions

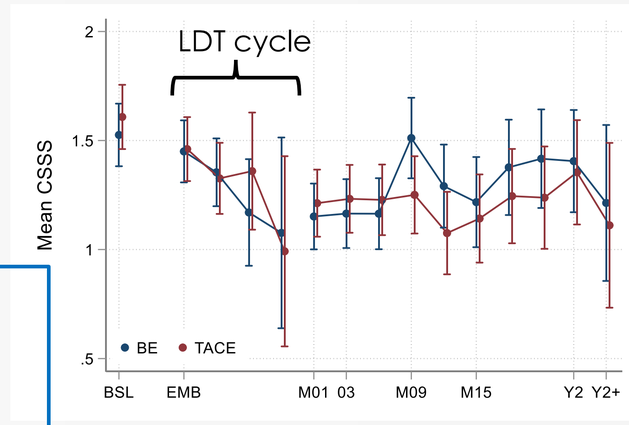
TAE and cTACE have similar oncologic efficacy.
TAE has more SAE's, DEE should not be used.
Further analyses of subgroups, correlatives and PRO's underway

No difference in hepatic- or extra-hepatic PFS





Sustained syndrome control to 2 years in both arms



Funded by a grant from Guerbet