Randomized Embolization Trial for NeuroEndocrine Tumors (RETNET):

A phase 2 randomized multicenter trial to compare hepatic progression-free survival following bland embolization, lipiodol chemoembolization, and drug-eluting bead chemoembolization of neuroendocrine liver metastases

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BACKGROUND

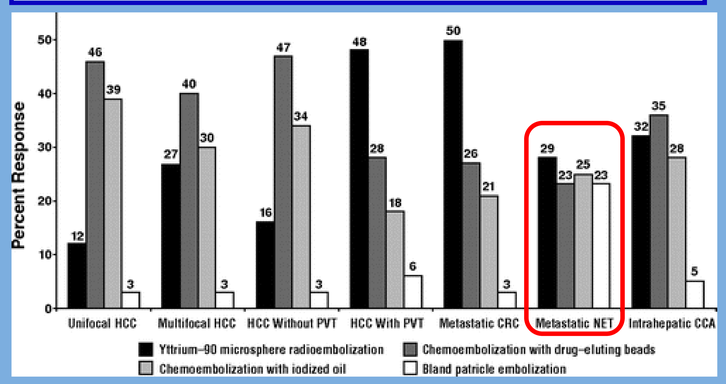
- Liver metastases occur in 9 out of 10 NET patients
- Most common, and often only, site of disease progression even when there are metastases elsewhere
- If not controlled, leads to death from liver failure
- NANETS/ENETS/NCCN Guidelines recommend embolotherapy by any technique for symptomatic or progressive liver metastases

EMBOLOTHERAPY

4 techniques in guidelines:

- Bland embolization with microspheres alone
- "Conventional" cTACE with Lipiodol-drug emulsion
- "DEB-TACE" with drug-eluting microspheres
- Radioembolization ("TARE") with yttrium-90 microspheres

All four techniques are used equally for NETS (Gaba 2012)



RESULTS OF EMBOLOTHERAPY

	Bland	Lipiodol	DEB	Y90
Median TTP range	6-17mo	10-34mo	14, 18 mo	4-20 mo
Median TTP average	11 mo	21 mo	16 mo	13 mo
2-year PFS	0-20%	20%-65%	No data	40% (one study)

Historical data suggests similar outcomes for the different embolotherapy techniques, which have never been compared in a controlled study.

It is possible that significant differences may exist in the domains of

1. Oncologic outcomes
2. Toxicity and adverse events
3. Patient-reported outcomes.

STUDY DESIGN

- RETNET is an open-label, multicenter, randomized comparison of three standard techniques of embolotherapy for neuroendocrine liver metastases
- 180 subjects will be randomized to 3 arms, equally (1:1:1)
- Eligible participants will have liver-dominant neuroendocrine tumor(s) that are symptomatic or progressive. Or, a liver tumor burden of >25% of the liver volume without the need for documented progression
- No concomitant anti-cancer therapy (other than octreotide analogs) is allowed

PRIMARY OBJECTIVE

- To estimate the duration of hepatic progression-free survival, or HPFS, in patients using bland embolization, cTACE, and DEB-TACE
- The primary hypothesis is that TACE will be nearly twice as durable as bland embolization, with a hazard ratio for HPFS of 1.78 or better

SECONDARY OBJECTIVES

1. Compare the interval between the cycles of embolotherapy
2. Estimate the symptom-free interval for patients with tumor-related symptoms using the Carcinoid Symptom Severity Scale
3. Compare patient-reported outcomes using the EORTC: QLQ-C3 & GI.NET21
4. Compare toxicities and adverse events
5. Compare progression-free survival (PFS) and duration of symptom control among patients with different histologic subtypes and tumor grade
6. Identify biomarkers (imaging, serum, and symptom) of treatment effect

USA sites:
Dana Farber
Northwestern
Memorial-Sloan Kettering CC
Vanderbilt
Med Coll Wisconsin
MD Anderson CC
Oregon HSU
LSUHSC
U Iowa
Moffitt CC
Stanford
UCSF
Emory
Montefiore (NY)

France:
Institut Gustav Roussy
Hôpitaux de Paris

Argentina:
Hospital Italiano, Buenos Aires

CommNETS (Canada/Australia/NZ)

REFERENCE
Chen JX, Rose S, White SB, et al. Embolotherapy for Neuroendocrine Tumor Liver Metastases: Prognostic Factors for Hepatic Progression-Free Survival and Overall Survival. Cardiovasc Intervent Radiol 2017 Jan;40:69-80

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