Locoregional Therapies in Metastatic Liver Carcinoma: Colorectal Carcinoma

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Disclosures

• Nothing to disclose
Based on your people skills, I strongly suggest you choose radiology for your medical specialty.
Overview

• Colorectal metastases facts/management
• Locoregional therapies in the liver for metastatic colorectal carcinoma (mCRC):
  – Thermal Ablation
  – Chemoembolization
  – Y-90 Radioembolization
Overview

- Other hepatic tumors for which locoregional therapy may play a role:
  - Hepatocellular carcinoma
  - Neuroendocrine tumor
  - Cholangiocarcinoma
  - Breast, lung, pancreas
Colorectal Metastases

- Metastases in 50% of those diagnosed with CRC
- Majority of disease related death related to metastasis
- Liver metastases cause majority of morbidity and mortality

Medical and Surgical Management mCRC

- Chemotherapy
- Surgical resection of primary tumor
- Surgical resection of hepatic metastases
Established Outcome Data: mCRC

- Untreated disease:
  - MS: 5 mo; 5 yr survival: 0%

- Chemotherapy alone:
  - MS: ~24 mo; 5 yr survival: ~0%

- Surgical resection (mets) + chemo:
  - Perioperative mortality: <5%
  - MS: > 40 mo; 5 yr survival: 24-58%
  - < 15% candidates for resection

Locoregional Therapy in mCRC

- Thermal Ablation
- Transarterial
  - Chemoembolization
  - Y-90 Radioembolization
Thermal Ablation

- Radiofrequency or Microwave
- CT or US guidance
- Goal is complete ablation of lesion with margin
- Best outcomes in those with:
  - Lesion size <3 cm
  - Solitary/fewer number of lesions
  - No extrahepatic disease
Thermal Ablation
Thermal Ablation

• 5 year survival (RFA) ~40 %, even in nonsurgical candidates
  – Surgical resection: 5 yr survival: 24-58%
• Some unresectable lesions, poor operative candidates
• Local recurrence rate higher than surgery:
  – As high as 40% for RFA vs 5-10% for resection

Thermal Ablation
Transarterial Therapies

• Delivery of chemo or radiation into the hepatic artery
  – Chemoembolization
  – Radioembolization

• Dual Blood supply to the liver
  – Hepatic artery
  – Portal vein
Transarterial Therapies

• Normal hepatocyte blood supply:
  – 75% portal vein
  – 25% hepatic artery

• Tumor blood supply: >90% supply from hepatic artery
Hepatic Dual Blood Supply

CT Hepatic Artery Injection: Metastases

CT Portal Vein Injection: Normal Parenchyma
DEB Chemoembolization

- Use of "drug eluting beads" is off label in US
- Injection of irinotecan loaded particles into the HA
- Particles lodge in arterioles and release chemo locally
DEB Chemoembolization

- Delivery of irinotecan to tumor is 2x that of IV
- Greater rate of tumor necrosis vs IV/IA
- Several studies show high rates of response with DEBIRI + infusional chemo
- RCT 74 patients with improved OS (22 vs 15 mo vs FOLFIRI alone)

Y-90 Radioembolization

- Injection of tiny radioactive particles into the hepatic artery
- Particles lodge in tumor arterioles and emit powerful radioactivity, selectively killing tumor cells
Yttrium-90

- Emits high energy beta particle
  - Avg tissue penetration: 2.5 mm

- Half life: 64.1 hours
  - >90% radiation dose delivered in 11 days
Y-90 Terminology

- SIRT: Selective Internal Radiation Therapy
- Radioembolization
- Y-90
Y-90: Rationale

- Hepatic metastases radiosensitive...so are normal liver cells
- Y-90 therapy also takes advantage of hepatic arterial supply to tumor cells
Y-90 Mechanism of Action

• Microspheres injected via HA
• Lodge in tumor arterioles
Indications

• SIR-Spheres: FDA approved for treatment of non-resectable mCRC
• Theraspheres: Used under HDE for non-resectable HCC
• Off label uses:
  – Cholangiocarcinoma
  – Neuroendocrine
  – Breast, lung, pancreas
Y-90 in mCRC: Who is a Candidate?

- Salvage/chemorefractory
  - Failure of multiple lines of chemo
  - Modest increase in OS (8.3 vs 3.5 mo)
  - Generally well tolerated, directed therapy limits systemic toxicity

Y-90 in mCRC: Who is a Candidate?

- Y-90 in combo with 2\textsuperscript{nd} line chemo
  - Failure of 1\textsuperscript{st} line therapy
  - Local tumor control with 2\textsuperscript{nd}/3\textsuperscript{rd} line tx
  - Increase time prior to changing chemo regimen
Y-90 in mCRC: Who is a Candidate

- 1\textsuperscript{st} line with chemotherapy

- SIRFLOX Trial
  - 530 pts randomized, FOLFOX\textsubscript{6} (+/- bev) vs SIRT + FOLFOX\textsubscript{6} (+/-bev)
  - Increase in liver PFS ~8 months (12.1 vs 20.5 mo)
  - >30\% decreased risk of liver progression
  - 3x increase in CR vs chemo alone
  - Overall PFS benefit not shown
Ideal Y-90 Candidate

- Liver dominant metastatic disease
- Tumor burden <60%
- Preserved liver function
  - Total bilirubin <2.0
- Good performance status
- Life expectancy >3 months
Y-90 Procedure

• Staged procedure
  – Shunt study: Tc-99m MAA
    • Hepatic artery mapping
    • Lung shunt fraction
    • Embolization of extrahepatic arteries
  – Lobar Y-90 therapy
    • Decreased risk of hepatic toxicity with lobar tx
Y-90 Shunt Study

- % MAA shunted from liver to the lung
- Extrahepatic uptake of radiotracer
Y-90 Therapy

- Calculate dose
  - Liver/tumor volumes
  - BSA
  - Lung shunt fraction
    - <20%
Y-90 Therapy

Acrylic shielding, low penetration of B particle in tissue and air
Y-90 Post Imaging

- SPECT CT
  - Post Y-90
Y-90 Post Imaging

• Comparison

Shunt Study

Y-90
Post Y-90: Follow Up

- Second lobe treatment: ~4 weeks following initial tx
- Follow up imaging
  - 8-12 weeks after last tx
  - Early follow up may not show treatment effect, may show psuedoprogression
Y90: Adverse Effects

- Mild abdominal discomfort
- Fatigue
- Fever/flu-like symptoms
- Elevated liver enzymes
- After Y-90 therapy:
  - Antibiotics, nausea medication, steroid pack, pepcid, pain medication
Y90: Rare Adverse Effects

- Severe abdominal pain, anorexia, weight loss
- GI ulceration (1-2%): non-target embolization
- Radiation cholecystitis
- Radiation pneumonitis: ? Lung shunt fraction
- Radioembolization induced liver disease
  - Jaundice and ascites 1-2 mo post tx
  - Rarely may lead to liver failure
Summary

- Locoregional therapies are important tools in the treatment of mCRC
  - Ablation of metastases
    - Similar outcomes to surgical resection
  - Chemoembolization
    - Improved OS in chemo naïve or >3 mo out from 1\textsuperscript{st} chemo
  - Y-90 Radioembolization
    - Outpatient procedure, acceptable safety profile, has the potential to improve PFS and OS