Multidisciplinary Treatment Strategies for Primary and Metastatic Liver Cancers

Ching-Wei D. Tzeng, M.D.
Assistant Professor
Surgical Oncology
University of Kentucky

Markey Cancer Center Affiliate Network
Annual Meeting
April 25, 2014
Topics

• Modern treatment options and updates

• Multidisciplinary treatment planning

• Services offered at UK/MCC

• Markey Cancer Center Affiliate Network
Types of Liver Cancer?

• Primary
  – Hepatocellular carcinoma (HCC)
  – Bile duct cancer (cholangiocarcinoma)

• Metastatic
  – Colorectal - most common
  – Neuroendocrine/carcinoid
  – Other GI cancers
  – Any solid tumor can go to liver (breast, melanoma, etc.)
Primary Liver Cancer

- More cases due to fatty liver disease
Primary Liver Cancer

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Liver and Intrahepatic Bile Duct Cancer

Percent of Cases by Stage:
- Localized (42%): Confined to Primary Site
- Regional (27%): Spread to Regional Lymph Nodes
- Distant (18%): Cancer Has Metastasized
- Unknown (13%): Unstaged

5-Year Relative Survival:
- Localized: 29.7%
- Regional: 10.9%
- Distant: 2.8%
- Unstaged: 5.6%

SEER 18 2004-2010, All Races, Both Sexes by SEER Summary Stage 2000

SEER.cancer.gov
Primary Liver Cancer: Risk Factors

• Cirrhosis
  – Hepatitis B or C
  – Excessive alcohol use

• NASH – non-alcoholic steatohepatitis
  – Obesity/Diabetes – Non-alcoholic fatty liver disease (NAFLD)
Primary Liver Cancer: Treatment Options

• Surgery
  – Resection vs. Transplant
• Locoregional Therapy (non-operative)
• Medical Therapy
  – Chemotherapy
  – Targeted therapy
• Radiation Therapy
  – External vs. Internal

• Must have multidisciplinary discussion upfront
Resection (Bile Duct Cancer)

- Removed 60% liver for bile duct tumor
TACE: Transarterial Chemoembolization

- Drug-eluting beads or direct chemo

Kalva, Gastrointest Cancer Res, 2011
Microwave Ablation

- Heat to kill tumor cells directly

www.surgical.covidien.com
Y90 Radioembolization

- Using blood flow to deliver radiation internally

www.sirtex.com
Transplantation for HCC: Rationale

• Most HCC multifocal
• Best oncologic treatment of whole liver
• Treats parenchymal disease: cirrhosis
• Restores normal hepatic function
Cirrhosis

Image provided by TA Aloia
Polycystic Liver Disease

Image provided by E Maynard
Metastatic Colorectal Cancer (CRC)

- ~50% metastatic at some point
- ≥20% CLM potentially resectable
Improved Survival From Better Chemo For CLM Since Mid-2000’s

Kopetz, JCO 2009
But Chemotherapy Is Not the Goal for Resectable CLM – Resection Should Be
Benefits of Multidisciplinary Management

• Maximizes use of multimodality therapy
• Upfront team consensus
• Prevents unilateral decision-making which may limit/eliminate options
  – Complications from resection of asymptomatic primary tumor
  – Treatment with extensive chemo with small future liver remnant
• Helps patients understand goals of therapy
• Simultaneous referrals to all specialties
Perioperative Chemotherapy for Colorectal Liver Mets (CLM)

- **Who needs it?**
  - Resectable – *Yes*, timing controversial
  - Borderline resectable – *Yes*, upfront
  - Initially unresectable – *Yes*, upfront

- **Positives:**

- **Downsides:**
Potential Advantages of Preoperative Chemotherapy

• Downsize and decrease extent of resection (save parenchyma for safety and future treatment)
• Margin control (R1=R0 resection in chemo responders)\(^1\)-\(^2\)
• Assess tumor response morphologically
• Predict outcomes with pathologic response
• Convert initially unresectable
• Guarantees at least some chemo for the pt

1. Pawlik, Ann Surg 2005
Potential Disadvantages of Preoperative Chemotherapy

• Chemotherapy-associated liver injury (CALI)
  – Usually from extended duration (>6 cycles)
  – FOLFOX – blue
• Increased postop morbidity
• FOLFIRI – yellow
  – Increased postop mortality

• Disease progression is not a “downside”
Blue Liver (Oxali)

a Whole liver with SOS
b Cut liver with SOS
c Sinusoidal dilatation

Zorzi, Br J Surg 2007
What is "Extended Duration" Preoperative Chemotherapy?

<table>
<thead>
<tr>
<th>Percent</th>
<th>a) 20% FLR</th>
<th>b) 30% FLR</th>
<th>Death from liver failure</th>
<th>PHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>PH = 0.006*</td>
<td>PH = 0.15</td>
<td>14/86 (16.3%)</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>PH = 0.49</td>
<td></td>
<td>2/86 (2.3%)</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
<td></td>
<td>4/78 (5.1%)</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td></td>
<td></td>
<td>1/78 (1.3%)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td>0/30 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td>0/5 (0.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Decreased PHI and No Deaths

Shindoh, Tzeng, Ann Surg Oncol 2013
What Can We Offer? A Modern Game Plan For Our Shared Patients
Parenchymal Sparing Resections

- Takes longer for the surgeon with more technical demands
- But better for the patient
Parenchymal Sparing Resections

- Saves liver tissue for future resections
- Reduces postop liver failure
- Preserves liver function for future chemo
- Easier postop course
Portal Vein Embolization

• Tricking the liver into growing before resection
Case 1: 55 yo male with metastatic rectal cancer. PS 0. Small FLR.

Baseline with 17% FLR (segments I, II, III)

Insufficient FLR: options?
1. Chemotherapy for life
2. Attempt resection (high risk of PHI or death)
3. PVE
Portal Vein Embolization (PVE)

Pre-PVE FLR (seg 1-3) 10% vs. Total Liver Volume

Post-PVE FLR (seg 1-3) 33% vs. Total Liver Volume
Case 1: 55 yo male with metastatic rectal cancer. PS 0. Small FLR.

Before PVE with 17% FLR (segments I, II, III)

After PVE with 33% FLR
Two-Stage Hepatectomy

- Convert initially unresectable into resectable by staging
Case 2: 51 yo male with synchronous liver metastases and low rectal cancer

• 13 synchronous CLM, involving 7 of 8 liver segments
  – initially unresectable → no surgical referral?
After FOLFOX Bevacizumab x4

Type I Morph Response (sharp margin, no enhancement)
After first stage partial left hepatectomy + proctectomy

After PVE extended to segment IV

FLR% (I, II, III) = 17%

FLR% (I, II, III) = 27%
• Second Stage: Extended Right Hepatectomy

• Finished last 8 of 12 cycles of chemo

• Alive NED 5 years later
Two-Stage Resection of Advanced Bilateral CLM

Cumulative Survival

Advanced Bilateral CLM
Two-Stage Completed (n = 47)

Advanced Bilateral CLM
Chemotherapy-Only (n = 62)

Advanced Bilateral CLM
Two-Stage Not Completed (n = 18)

Months

Brouquet A J Clin Oncol 2011
Reverse Approach Sequencing

• Take care of life-limiting issue first – liver mets
Case 3: 36 year old man with synchronous non-obstructing primary CRC

- Two Metastases: Seg 4/8 (encasing MVH) + Seg 6
  - If this progresses, it may become unresectable
  - Why do we have to take out primary first?
Synchronous Liver Metastases and Rectal Cancer

Traditional Approach

1. Assessment
2. Chemoradiation
   - 5 weeks
3. Proctectomy
   - 6 weeks
   - 1 week
   - 4 weeks
4. Systemic Chemotherapy
5. Liver Resection

Reverse Approach

1. Assessment
2. Periop Systemic Chemotherapy
3. Liver Resection
4. Chemotherapy + Chemoradiation
5. Proctectomy

>15 weeks without effective systemic chemo
(only 5-FU or Xeloda)

Same Case 3: Synchronous CLM and Non-Obstructing Sigmoid Primary

After FOLFOX-6 + Bevacizumab → Type I Morph Response (sharp margin, no enhancement)
• Pre-PVE FLR (seg 1-3) =10% of Total Liver Volume (“initially unresectable”)
• Post-PVE FLR (seg 1-3) =33% of Total Liver Volume

• Extended R hep
• Path: < 5 % viable tumor; neg margin (4 mm from mucin pools)
• Sigmoid colectomy 6-8 weeks later
Team Approach at Markey Cancer Center

• Multidisciplinary Tumor Board twice weekly
  – Surgery (Transplant, HPB, Surgical Oncology)
  – Medical Oncology
  – Radiation Oncology
  – Interventional Radiology
  – GI Medicine (Endoscopy, Hepatology)
  – Pathology
  – Diagnostic Radiology
  – Clinic coordinators
  – Dietician
  – Social workers
New UK Markey Cancer Center Multidisciplinary Liver Tumor Clinic

- All patients with liver tumors (benign or cancer) will be seen at MCC
- Staffed by multiple specialties
  - Convenient for patients
  - Convenient for referring doctors
  - Consensus treatment plan given to patients and referring doctors
- Many aspects of plan (other than specialized procedures) can be done at Network Centers
- Unique collaboration among specialties
Conclusions

• Multidisciplinary treatment planning is most helpful upfront at presentation

• MCC relies heavily on its partners to deliver components of the multimodality therapy closer to home

• Together, we can increase the number of patients with optimized treatment plans
Multidisciplinary Treatment Strategies for Primary and Metastatic Liver Cancers

Ching-Wei D. Tzeng, M.D.
Assistant Professor
Surgical Oncology
University of Kentucky

Markey Cancer Center Affiliate Network
Annual Meeting
April 25, 2014