Chemosaturation Using Percutaneous Hepatic Perfusion: Pre-Embolization of GI Branches in a Phase 3 Clinical Trial

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DISCLOSURES

Chemosaturation is not FDA approved. It is currently performed only under IDE/HDE. FDA approval is currently pending.

FM & CN – Delcath Consultants and prior Honorariums
Chemosaturation – The Concept

“Isolate an Organ”

Then Infuse with High-dose Chemotherapy
Chemosaturation Using the PHP System

Isolation  Saturation  Filtration
Chemosaturation

- IVC venogram
- Back filling of hepatic veins
  - Left usually does not fill
- No leak around cranial balloon into right atrium
## Melphalan Dosing

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Dosing Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple myeloma</td>
<td>0.25 mg/kg(^1)</td>
</tr>
<tr>
<td>Chemoembolization</td>
<td>0.62 mg/kg (25 mg/m(^2))(^2)</td>
</tr>
<tr>
<td>Isolated hepatic perfusion</td>
<td>1.5 mg/kg(^3)</td>
</tr>
<tr>
<td>Percutaneous hepatic perfusion</td>
<td>3.0 mg/kg</td>
</tr>
<tr>
<td>Myeloablation</td>
<td>2.5-3.5 mg/kg (100-140 mg/m(^2))(^1)</td>
</tr>
</tbody>
</table>
A Phase-III Random Assignment Trial Comparing Percutaneous Hepatic Perfusion with Melphalan (PHP-mel) to Standard of Care for Patients with Hepatic Metastases from Metastatic Ocular or Cutaneous Melanoma. (LBA #8512)

Authors: JF Pingpank, MS Hughes, HR Alexander, MB Faries, JS Zager, RE Royal, ED Whitman, CW Nutting, GP Siskin, SS Agarwala

June 5, 2010
ASCO
Chicago, Illinois
Phase III Random-Assignment

**PHP vs. BAC**

Accrual goal: 92 patients
(Cross-over at Hepatic progression)
10 Institutions

Melphalan dose: 3.0 mg/kg

Primary endpoint: Hepatic PFS

Secondary endpoints:
- Response rates, DFS with best available therapy
- Response rates for patients treated with PHP
Treatment Schema

On Study Evaluation/Randomization

Interval Evaluation (Baseline, 6-weeks, 12 weeks, 20 weeks, 28 weeks, 36 weeks)

Treatments 1 through 6
- Melphalan
- Angiogram (Celiac, SMA)
- GDA assessment (Treatment #1)

4-5 Weeks 4-5 Weeks 4-5 Weeks 4-5 Weeks 4-5 Weeks 4-5 Weeks

24-30 weeks

Post Treatment Follow-up
Melphalan GI Toxicity

- The GI tract is extremely sensitive to melphalan
- Exposure results:
  - Ulceration/perforation
  - Gastritis
  - Diarrhea
Arterial Isolation

- Pre-treatment Collateral Vessel assessment and embolization
- Goals
  - Protect Extrahepatic GI structures
  - Simplify CS administration
Results: Vessels Embolized

- None: 18 patients
- Right Hepatic Artery: 2 patients
- Left Hepatic Artery: 5 patients
- Right Gastric Artery: 11 patients
- Left Gastric Artery: 8 patients
- Gastroduodenal Artery: 70 patients

Patients (%)
Results: Number of Embolizations

- None: 18 patients (18%)
- Solitary: 66 patients (66%)
- Two or More: 16 patients (16%)
Results: Embolization Cycle

- Cycle 3: 2 patients
- Cycle 2: 10 patients
- Cycle 1: 72 patients
Hepatic Arterial Redistribution

Left Hepatic?

GDA

Right Gastric
Hepatic Arterial Redistribution
### Treatment Associated Toxicities

### Angiographic Complications
- Coil migration 1 pt (1.5%)

### GI Toxicities
- Gastric Ulcer/Perforation 1 pt (1.5%)

### Treatment Related Toxicity, Grade 3–4 and Grade 5 (n=116 treatments)

<table>
<thead>
<tr>
<th>Category</th>
<th>Grade 3–4 (n,%)</th>
<th>Grade 5 (n,%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematologic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>71 (61.2%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>86 (74.1%)</td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>54 (46.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated AST</td>
<td>14 (12.1%)</td>
<td></td>
</tr>
<tr>
<td>Elevated ALT</td>
<td>6 (5.2%)</td>
<td></td>
</tr>
<tr>
<td>Hyperbilirubinemia</td>
<td>8 (6.9%)</td>
<td>1 (0.86%)</td>
</tr>
<tr>
<td>Increase AP</td>
<td>6 (5.2%)</td>
<td></td>
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</tbody>
</table>
Conclusions

• Hepatic arterial mapping with collateral arterial embolization is essential prior to CS-PHP
• The most commonly embolized vessels are the GDA, RGA, and LGA branches
• Dedicated pre-treatment angiography essential to locate and eliminate “new” collateral vessels if they arise prior to repeat therapy
Recommendations

- Pre-CS Hepatic Mapping should be performed 1-2 weeks prior to planned initial CS treatment
- Hepatic Arterial Redistribution simplifies CS treatment and should be utilized when feasible
- *Highly recommend complete extrahepatic collateral embolization*
  - GDA
  - RGA
  - Misc. Gastric Collaterals
  - Super Duodenal?

Y90 Experience
Thank You!

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