Hepatocellular Carcinoma

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

INITIAL EVALUATION

- History and physical.
- CBC with differential; liver function tests; creatinine; electrolytes; PT/INR; lipid profile, Hemoglobin A1C
- Viral labs if not known (HBV core and surface antibody (Ab); HCV Ab and RNA if Ab positive; HIV serology if HCV Ab positive or HBV core Ab positive); alpha-fetoprotein (AFP).
- Triple Phase CT or MRI of abdomen and pelvis; CT chest – PET scan.
- Consider consult if indicated:
  - Hepatology for chronic liver disease or HBV treatment
  - Infectious Diseases for HCV or HIV treatment.

Liver-only disease

- Resectable\(^1,2\) or transplantable\(^3\)?

Yes → Surgery\(^6\)

No → See Page 2 for unresectable tumors

Isolated metastasis?\(^4\)

Yes

- Performance status 0-2\(^5\), CLIP\(^5\) 0-3, and Child-Pugh A-B\(^5\) and bilirubin less than or equal to 2 mg/dL

- Systemic treatment (sorafenib)

- Best supportive care

No

- Performance status\(^5\) greater than 2, CLIP\(^5\) 4-6, or Child-Pugh C\(^6\) or bilirubin greater than 2 mg/dL\(^7\)

Further treatment based on primary liver lesions

Metastatic disease

Resectable\(^1,2\) or transplantable\(^3\)?

Yes → Surgery\(^6\)

No → See Page 2 for unresectable tumors

TREATMENT

Yes → Treat isolated metastasis first

SURVEILLANCE

- History and physical
- CBC with differential, liver function tests (LFTs), alpha-fetoprotein (AFP), electrolytes, PT/INR
- Triple phase CT abdomen, CT chest every 4 months for 2 years, then every 6 months for 3 years, then annually. Favor MRI for frequent imaging if long term survival anticipated

1 Consider biomarkers (see MDACC Approved Hepatocellular Biomarkers: https://www.mdanderson.org/content/dam/mdanderson/documents/for-physicians/algorithms/clinical-management/clin-management-biomarkers-web-algorithm.pdf

2 Minor or Major Resection based on:
   - Minor Resection: Child-Pugh A, normal liver function tests (bilirubin less than or equal 1.0 mg/dL), absence of ascites, and platelet count greater than 100,000 K/microliter
   - Major Resection: Same as minor resection plus absence of portal hypertension, portal vein embolization (PVE) for a small future liver remnant.

3 Milan criteria; criteria for eligibility for liver transplantation for patients with hepatocellular carcinoma and cirrhosis: the presence of a tumor 5 cm or less in diameter in patients with single hepatocellular carcinomas, or no more than three tumor nodules, each 3 cm or less in diameter, in patients with multiple tumors, and without macrovascular invasion per imaging studies.

4 See Appendix A for Eastern Cooperative Oncology Group (ECOG) performance status.

5 See Appendix B for determination of Cancer of Liver Italian Program (CLIP) Investigators score.

6 Child-Pugh – refer to Appendix C for Child-Pugh scores

7 Treatment may be considered in select cases with bilirubin 2-3 mg/dL

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Note: Consider clinical trials as treatment options for eligible patients.

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Approved by Executive Committee of the Medical Staff 04/25/2017
### CLINICAL PRESENTATION FOR UNRESECTABLE TUMORS

<table>
<thead>
<tr>
<th>Performance status 0-2(^1), CLIP(^2) 0-3, Child-Pugh(^3) A-B and bilirubin less than or equal to 2 mg/dL</th>
<th>Well defined lesions?</th>
<th>Single lesion 25-50% tumor burden</th>
<th>Multiple lesions greater than 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Single lesion greater than 3 cm</td>
<td>Tumor Thrombus</td>
<td>Any tumor burden above with branch portal vein or hepatic vein</td>
</tr>
<tr>
<td>No</td>
<td>Multiple lesions (up to 3-4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease Morphology on imaging indicated infiltrative/ill-defined disease or there is major vein involvement or disease burden greater than 50%</td>
<td>Performance status greater than 2(^1), CLIP(^2) 4-6, Child-Pugh(^3) C or bilirubin greater than 3 mg/dL(^4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### STAGING

- Up to 3 lesions that are less than or equal to 3 cm in size
- Single lesion greater than 3 cm
- Overall tumor burden less than or equal to 25%
- Multiple lesions (up to 3-4)

### TREATMENT\(^5\)

1. Ablation
2. TACE
3. Combination of ablation and TACE when clinically appropriate
4. Radioembolization
5. Radiation therapy
6. Neoadjuvant PIAF when clinically appropriate

- 1. TACE
- 2. Combination of TACE and ablation when appropriate
- 3. Radioembolization
4. Radiation therapy
5. Neoadjuvant PIAF when clinically appropriate

- 1. Radioembolization
- 2. TACE in select cases where lesions grouping allows for selective TACE
- 3. Neoadjuvant PIAF when clinically appropriate

- 1. Radioembolization
- 2. TACE in select cases where lesions grouping allows for selective TACE
- 3. Radiation therapy
- 4. Neoadjuvant PIAF when clinically appropriate

### RE-STAGING WORKUP

- History and physical
- CBC with differential; liver function tests; AFP; electrolytes
- Triple phase CT abdomen and pelvis, and CT chest every 2 months until stable disease, then every 3 months for 2 years, then every 6 months for 3 years, then annually. Favor MRI for frequent imaging if long term survival anticipated

### CLINICAL PRESENTATION

- Performance status 0-2, CLIP\(^2\) 0-3, Child-Pugh\(^3\) A-B and bilirubin less than or equal to 2 mg/dL

### TREATMENT

- Treatment options based on feasibility and safety. If disease morphology on imaging indicated infiltrative/ill-defined disease or there is major vein involvement consider adding therapy (sorafenib) as a stand alone option or in combination with local therapy if feasible

---

\(^1\) See Appendix A for ECOG performance status

\(^2\) CLIP – refer to Appendix B for determination of CLIP score

\(^3\) Child-Pugh – refer to Appendix C for Child-Pugh scores

\(^4\) Treatment may be considered in select cases with bilirubin 2-3 mg/dL

\(^5\) Treatment options based on feasibility and safety. If disease morphology on imaging indicated infiltrative/ill-defined disease or there is major vein involvement consider adding therapy (sorafenib)
APPENDIX A: Eastern Cooperative Oncology Group (ECOG) Performance Status Criteria

<table>
<thead>
<tr>
<th>Grade</th>
<th>Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction (Karnofsky 90-100)</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, i.e., light housework, office work (Karnofsky 70-80)</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours (Karnofsky 50-60)</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self-care, confined to bed or chair more than 50% of waking hours (Karnofsky 30-40)</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry out any self-care. Totally confined to bed or chair (Karnofsky 10-20)</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>

APPENDIX B: Clip Scoring System

<table>
<thead>
<tr>
<th>Variables</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child-Pugh Stage</td>
<td>A</td>
<td>B</td>
<td>C</td>
</tr>
<tr>
<td>Tumor morphology</td>
<td>Uninodular and extension less than or equal to 50%</td>
<td>Multinodular and extension less than or equal to 50%</td>
<td>Massive or greater than 50%</td>
</tr>
<tr>
<td>AFP</td>
<td>Less than 400 ng/dL</td>
<td>Greater than or equal to 400 ng/dL</td>
<td></td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

APPENDIX C: Child-Pugh Score

<table>
<thead>
<tr>
<th>Chemical and Biochemical Parameters</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>1 - 2</td>
<td>3 - 4</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Slight</td>
<td>Moderate</td>
</tr>
<tr>
<td>Albumin</td>
<td>Greater than 3.5 g/dL</td>
<td>2.8 – 3.5 g/dL</td>
<td>Less than 2.8 g/dL</td>
</tr>
<tr>
<td>Prothrombin time prolonged</td>
<td>1 – 4 seconds</td>
<td>4 – 6 seconds</td>
<td>Greater than 6 seconds</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>1 – 2 mg/dL</td>
<td>2 – 3 mg/dL</td>
<td>Greater than 3 mg/dL</td>
</tr>
<tr>
<td>For primary biliary cirrhosis</td>
<td>1 – 4 mg/dL</td>
<td>4 – 10 mg/dL</td>
<td>Greater than 10 mg/dL</td>
</tr>
</tbody>
</table>

Class A = 5 to 6 points
Class B = 7 to 9 points
Class C = 10 to 15 points

Hepatocellular Carcinoma

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SUGGESTED READINGS

Child-Pugh score

CLIP score

Neoadjuvant Chemotherapy

Radiofrequency Ablation (RFA)


Radiation therapy

Surgery


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SUGGESTED READINGS - continued

Surgery (Continued)


Systemic Therapy (sorafenib)

This practice guideline is based on majority expert opinion of the Gastrointestinal Center Faculty at the University of Texas, MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following medical oncologists, radiation oncologists, surgical oncologists, and interventional radiologists:

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