### Selected Ongoing Trials in Hepatocellular Carcinoma

<table>
<thead>
<tr>
<th><strong>Resectable Disease</strong></th>
<th><strong>Intermediate Stage</strong></th>
</tr>
</thead>
</table>
| *CheckMate -9DX: Nivolumab in patients with high risk of recurrence (NCT03383458)*  
  Phase 3, Primary endpoint: RFS | CheckMate -74W: Nivolumab + ipilimumab + TACE (NCT04340193)  
  Phase 3, Primary endpoints: TTP and OS |
| *EMERALD-2: Durvalumab ± bevacizumab in patients with high risk of recurrence after curative treatment (NCT03847428)*  
  Phase 3, Primary endpoint: RFS | *EMERALD-1: TACE + durvalumab and bevacizumab in patients with locoregional HCC not amenable to curative therapy (NCT03778957)*  
  Phase 3, Primary endpoint: PFS |
| *IMbrave050: Atezolizumab + bevacizumab vs active surveillance in patients with high risk of recurrence after surgical resection or ablation (NCT04102098)*  
  Phase 3, Primary endpoint: RFS | *LEAP-012: Lenvatinib + pembrolizumab + TACE in patients with incurable/non-metastatic HCC (NCT04246177)*  
  Phase 3, Primary endpoint: PFS and OS |
| *KEYNOTE-937: Pembrolizumab in patients with HCC and complete radio-logical response after surgical resection or local ablation (NCT03867084)*  
  Phase 3, Primary endpoint: RFS and OS | *TACE-3: Nivolumab + TACE (DC Bead eluting doxorubicin) for patients with intermediate stage HCC (NCT04268888)*  
  Phase 2/3, Primary endpoints: OS and TTTP |
| Lenvatinib in patients with high-risk HCC post liver transplantation (NCT04168944)  
  Phase 2/3, Primary endpoint: TFS | TACE vs SBRT in patients with residual or recurrent disease after TACE (NCT02762266)  
  Phase 3, Primary endpoint: FFLP |
| *Cemiplimab (NCT03916627)*  
  Phase 2, Primary endpoint: STN at time of surgery | *IMMUTACE: Nivolumab + TACE (NCT03572582)*  
  Phase 2, Primary endpoint: ORR |
| *Nivolumab ± ipilimumab (NCT03222076)*  
  Phase 2, Primary endpoint: Incidence of AEs | *LANCE: Lenvatinib + TACE in patients with high risk of postoperative recurrence (NCT03838796)*  
  Phase not applicable, Primary endpoint: DFS |
|  | *TACE + durvalumab + tremelimumab (NCT03638141)*  
  Phase 2, Primary endpoint: ORR |

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40
**Advanced Stage**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Description</th>
<th>Phase</th>
<th>Primary endpoint(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CheckMate -9DW:</strong> Nivolumab + ipilimumab (NCT04039607)</td>
<td>Phase 3, Primary endpoint: OS</td>
<td>STOP-HCC: Y90 glass microspheres + sorafenib vs sorafenib (NCT01556490)</td>
<td>Phase 3, Primary endpoint: OS</td>
</tr>
<tr>
<td><em>Camrelizumab (SHR-1210) + apatinib vs sorafenib (NCT03764293)</em></td>
<td>Phase 3, Primary endpoints: OS and PFS</td>
<td>Tislelizumab (BGB-A317) vs sorafenib (NCT03412773)</td>
<td>Phase 3, Primary endpoint: OS</td>
</tr>
<tr>
<td><em>COSMIC-312:</em> Cabozantinib + atezolizumab vs sorafenib (NCT03755791)</td>
<td>Phase 3, Primary endpoint: PFS and OS</td>
<td>Durvalumab ± tremelimumab vs durvalumab vs tremelimumab vs durvalumab + bevacizumab (NCT02519348)</td>
<td>Phase 2, Primary endpoint: safety</td>
</tr>
<tr>
<td><strong>HIMALAYA:</strong> Durvalumab ± tremelimumab vs sorafenib (NCT03298451)</td>
<td>Phase 3, Primary endpoint: OS</td>
<td><em>Nivolumab + lenvatinib (NCT03841201)</em></td>
<td>Phase 2, primary endpoints: ORR and safety</td>
</tr>
<tr>
<td><strong>LEAP-002:</strong> Lenvatinib + pembrolizumab vs lenvatinib (NCT03713593)</td>
<td>Phase 3, Primary endpoints: PFS and OS</td>
<td>RESCUE: Camrelizumab (SHR-1210) + apatinib (NCT03463876)</td>
<td>Phase 2, Primary endpoint: ORR</td>
</tr>
<tr>
<td><em>ORIENT-32:</em> Sintilimab + IBI305 vs sorafenib (NCT03794440)</td>
<td>Phase 3, Primary endpoints: OS and ORR</td>
<td><em>Regorafenib + pembrolizumab (NCT03347292)</em></td>
<td>Phase 1, Primary endpoint: safety</td>
</tr>
<tr>
<td><em>Sorafenib ± SBRT vs sorafenib (NCT01730937)</em></td>
<td>Phase 3, Primary endpoint: OS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* More information and current enrollment status for the clinical trials listed here can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov). * Recruiting AE: adverse event; BSC: best supportive care; DFS: disease free survival; FFLP: freedom from local progression; HCC: hepatocellular carcinoma; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; RFS: recurrence-free survival; SBRT: stereotactic body radiation therapy; STN: significant tumor necrosis; TACE: transarterial chemoembolization; TFS: tumor free survival; TTTP: time to TACE progression; Y90: yttrium 90.

**Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40**
What special training is necessary to prepare my staff for a local outbreak of COVID-19?

Train staff on:
• Symptom recognition
• Screening procedures
• Use of Standard Precautions and personal protective equipment (PPE)
• Obtaining SARS-COV2 testing for patients according to current testing guidelines
• Protocols for triaging and assessing patients quickly
• Identifying and referring patients, families, and coworkers to telephone-based mental health services

What workplace changes should be made to prepare for a local outbreak of COVID-19?

• If necessary, obtain additional PPE for staff members who do not usually use it.
• Limit facility access to one point of entry, if possible. Vendors, minimal ancillary services, most or all visitors, and people younger than age 18 should be denied access.
• Consider remote or virtual support services.
• Establish outside triage stations with social distancing of six feet apart to screen patients and visitors for COVID-19 symptoms and fever before appointments.
• Install barriers or social distancing mechanisms at front desks if screening is not conducted outside of the facility.
• Convert waiting areas to allow for distancing of at least six feet (eg, move chairs, cordon off every other chair).
• Convert open infusion suites to semi-private spaces with at least six feet distance between patients and/or use available curtains as a barrier between patients.
• Suspend (or move to a virtual platform) all onsite group and patient activities (eg, yoga, education seminars, support groups).

What patient scheduling changes should be made while pandemic restrictions exist?

• Due to reduced waiting areas, the number of appointments may have to be decreased or the time between appointments may have to be increased.
• Postpone routine follow-up visits of patients not on active cancer treatment. This includes 6-month and 12-month survivorship visits.
• Schedule brief, remote check-ins with patients on maintenance therapies to ensure that they have sufficient drug supplies; provide instructions on when they should call their provider.
• Institute direct telecommunication for survivorship check-ins. Create a timeline over the next months to schedule calls.
• Communicate COVID-19 information and the rationale for changes in appointments via direct telecommunication, websites, and patient portals.
• Consider home collection of routine lab samples instead of patient visits into the clinic. Results can be communicated via telephone.
• For areas not yet impacted by widespread, local transmission, postpone nonurgent visits so urgent visits can be scheduled more immediately.
• Use telemedicine for patients not requiring a physical exam, treatment, or in-office diagnostics.
• Ask patients to use telephone triage, patient portals, online assessment tools, or to call and speak with a staff member.
• Conduct remote check-ins to monitor high-risk patients’ symptoms

How should clinical trial investigators respond to the COVID-19 pandemic?

• ASCO acknowledges that conducting clinical trials will be particularly challenging during this time.
• The FDA has issued guidance on management of clinical trial patients during the coronavirus pandemic.
• The National Cancer Institute has issued guidance on the NCI Central Institutional Review Board website including advisories and FAQs.

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40
### Guideline Recommendations for HCC Systemic Therapies

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40

#### Targeted Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication/Status</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sorafenib</strong></td>
<td>First-line treatment of unresectable HCC Approved; NCCN Category 1 (Child–Pugh A) and 2A (B7) (NCCN also recommends as second-line option; Category 2A [Child–Pugh A or B7])</td>
<td>400 mg 2x/d w/o food; treatment interruption and/or dose reduction for possible AEs: 400 mg 1x/d or 400 mg every other d</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lenvatinib</strong></td>
<td>First-line treatment of unresectable HCC Approved; NCCN Category 1 (Child–Pugh A) (NCCN also recommends as second-line option; Category 2A [Child–Pugh A])</td>
<td>12 mg 1x/d for patients ≥60 kg or 8 mg 1x/d for patients ≤60 kg; dose modification may be needed for patients with renal or hepatic impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Regorafenib</strong></td>
<td>Second-line setting following treatment with sorafenib Approved; NCCN Category 1 (Child–Pugh A)</td>
<td>160 mg orally; 3 wk on, 1 wk off (4-wk cycle)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cabozantinib</strong></td>
<td>Second-line setting following treatment with sorafenib Approved; NCCN Category 1 (Child–Pugh A)</td>
<td>60 mg/d (dose studied in phase 2 and 3 trials)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ramucirumab</strong></td>
<td>Second-line setting following treatment with sorafenib Approved; NCCN Category 1 (AFP≥ 400 ng/mL)</td>
<td>8 mg/kg IV every other wk</td>
</tr>
</tbody>
</table>

#### Toxicity Considerations

**TKIs (sorafenib, lenvatinib, regorafenib, cabozantinib)**
- Watch for events such as hypertension or palmar-plantar erythrodysesthesia
- Monitor for hypertension, hemorrhage

**Ramucirumab**
- Monitor for hypertension, hemorrhage
**Guideline Recommendations for HCC Systemic Therapies**

**Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40**

### Toxicity Considerations

irAEs can occur with the use of checkpoint inhibitors.11,12,14,15,16

- irAEs can affect any organ site at any time; monitor for immune-related fatigue, pruritus, diarrhea, rash, and hepatic events

- Note patients in the IMbrave150 trial, testing atezolizumab with bevacizumab, were carefully screened for bleeding risk, varices had to be treated prior to enrollment, and endoscopies had to be performed within 6 months prior to the start of the study

- Consult available literature (product labelling, ASCO guidelines) for guidance on management, including for hepatic irAEs

### ICI and Combinations

<table>
<thead>
<tr>
<th>Agent Indication/Status</th>
<th>Dosage</th>
</tr>
</thead>
</table>
| **Atezolizumab + bevacizumab**<sup>2,10,11</sup>  
First-line treatment of advanced or metastatic HCC | Atezo 1,200 mg IV + bev 15 mg/kg IV every 3 wk (dose studied in phase 3 trial) |
| **Nivolumab**<sup>2,12</sup>  
Second-line setting following treatment with sorafenib (Child Pugh A or B)  
(NCCN also recommends as first-line option if ineligible for TKIs or other antiangiogenic agents) | 240 mg every 2 wk or 480 mg every 4 wk |
| **Pembrolizumab**<sup>2,13,14</sup>  
Second-line setting following treatment with sorafenib | 200 mg every 3 wk (dose studied in phase 2 trial) |
| **Nivolumab + ipilimumab**<sup>2,12,15</sup>  
Second-line setting following treatment with sorafenib or other checkpoint inhibitor | 1 mg/kg IV nivolumab + 3 mg/kg IV ipilimumab every 3 wk After 4 doses of combination therapy, administer nivolumab as single agent |

**Agent Indication/Status**

Liver Cancer: Resources For Your Patients

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40

- Blue Faery’s new Patient Resource Guide for Liver Cancer is available for download at https://www.bluefaery.org
- Other patient resources:
  - https://www.cancer.gov/types/liver
  - https://www.cancer.net/cancer-types/liver-cancer
  - https://liverfoundation.org/for-patients/resources
  - https://www.nccn.org/patients/guidelines/content/PDF/hepatobiliary-patient.pdf
Liver Cancer: Resources For Your Patients

### What is a clinical trial?

- A clinical trial is a research study that tests whether a new treatment is safe, effective, and better than the standard treatment. Clinical trials are an essential step in developing new and better treatments for cancer. Almost every cancer treatment patients receive today is the result of a clinical trial.

### What can I gain from participating in a clinical trial?

- Patients who participate in clinical trials can be some of the first to get a treatment before it is available to the public.
- For some patients, a clinical trial may be the best or only treatment option available.
- Other patients volunteer for clinical trials because they know that these studies are a way to contribute to progress in treating HCC.

### What are some of the possible risks associated with taking part in a clinical trial?

- There are some risks with a clinical trial, including possible side effects and the chance that the new treatment may not work.
- People are encouraged to talk with their healthcare team about the pros and cons of joining a specific clinical trial.

### What if I’m given a placebo or “sugar pill” instead of a real treatment?

- Placebos are rarely used in clinical trials. When they are used, they are usually combined with the standard treatment you would receive if you weren’t in the trial.
- If you are considering participation in a clinical trial, you will be told whether it involves use of a placebo.
- Unless a particular cancer has no available treatment, you will always receive an active treatment.

### How do I find a clinical trial?

- To find clinical trials specific to your diagnosis, talk with your doctor or visit clinicaltrials.gov.

---

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40
Case 1

- 62-year-old woman with NASH cirrhosis
- Child–Pugh A; AFP 134 ng/mL
- No ascites or encephalopathy
- ECOG PS 0
- MRI shows multifocal HCC (LR-5) with four lesions, largest 5.6 cm with invasion into the right portal vein

First-Line Options
- Sorafenib
- Lenvatinib
- Atezolizumab + bevacizumab (recently approved)

Enrollment in a Clinical Trial (Examples of Phase 3 Trials)
- Checkpoint inhibitor + TKI (ie, COSMIC-312), LEAP-002
- PD-1/L1 inhibitor + CTLA-4 inhibitor (ie, HIMALAYA, CheckMate -9DW)

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40
**Case 2**

- 60-year-old Asian man with chronic HBV
- MRI shows enlarging 8-cm right lobe tumor, HCC (LR-5), with two satellite lesions and new right branch portal vein tumor thrombus
- Child–Pugh A
- ECOG PS 0
- AFP level 130 ng/mL
- Started on sorafenib 400 mg twice daily (standard dose)
  - Patient required dose reduction to 200 mg once daily due to HFSR
  - Treated for 3 months, but then progressed

**Selecting a Second-Line, Targeted-Therapy Option:**
- Consider AE profile, AFP levels, liver function, comorbidities, and prior treatment history
- Regorafenib
  - Research in patients who cannot tolerate sorafenib is needed
- Ramucirumab
  - Not indicated for AFP levels <400 ng/mL
- Cabozantinib
  - Allowed ≤2 lines of prior therapy
  - Favorable data in patients with HBV

**Selecting an Immunotherapy Option:**
- Consider for patients who have not received immunotherapy in first-line
- Consider if:
  - Rapid progression and/or intolerance to TKI first-line therapy
  - Increasing degrees of hepatic dysfunction
  - Contraindications to antiangiogenic therapy (eg, non-healing wounds, active venous thromboembolism, bleeding complications)
- Prospective cohort and retrospective case series show acceptable safety and efficacy of nivolumab in Child–Pugh B HCC\(^1,2\)

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40
Case 3

- 59-year-old man with NASH and compensated cirrhosis
- Found to have incidental liver mass on imaging
- MRI shows 6.5-cm LR-5 lesion with two satellite nodules
- No vascular invasion and no metastatic disease
- Child–Pugh A; Bili 0.9, Alb 3.7, INR 1.0
- ECOG PS 0

Locoregional Therapy
- TACE
- TARE

Clinical Trials of Multimodal Combinations
- Checkmate -74W
- EMERALD-1
- LEAP-012
- TACE-3

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40
Case 4

- 56-year-old man with chronic HBV, on tenofovir, and compensated cirrhosis
- Undergoing HCC surveillance and found to have liver mass
- MRI shows 3.3-cm LR-5 lesion in segment VI
- Child–Pugh A; Bili 0.7, Alb 4.0, INR 1.0
- Platelet count 217
- ECOG PS 0
- Patient undergoes robotic liver resection without complication
- Returns to clinic, at which time you reinforce risk of recurrence

Active Surveillance

Clinical Trials of Adjuvant Immunotherapy

- EMERALD-2
- Checkmate - 9DX
- IMbrave050
- KEYNOTE -937

Access the activity, “Patient Stories From the HCC CaseBook: Expert Guidance on Optimizing Outcomes and Care With Newly Available and Emerging Therapies,” at PeerView.com/VBH40