



CASES

INSIGHTS INTO HEPATOCELLULAR CARCINOMA

Virtual Platform

March 15, 2021

Insights From Community Oncologists From the
Pacific Northwest, USA

HOW TO NAVIGATE THIS REPORT



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Report Snapshot	
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Topline Takeaways and Strategic Recommendations	
Key Insights and Discussion Summary	
<ul style="list-style-type: none">• First-line treatment for advanced HCC• First-line discussion overview• Second- or subsequent-line treatment for advanced HCC• Second-line discussion overview	
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STUDY OBJECTIVES

To gain advisors' perspectives on

- > Current treatment practices regarding therapy of unresectable advanced HCC
- > Current treatment practice attitudes toward recently introduced and upcoming agents

REPORT SNAPSHOT: SESSION OVERVIEW



A moderated roundtable discussion was held with community oncologists from the Pacific Northwest region of the United States in a virtual setting on **March 15, 2021**

Disease state and data presentations were led by **Dr Tanios Bekaii-Saab** from the Mayo Clinic in Phoenix, Arizona, in conjunction with content developed by the Aptitude Health clinical team

Insights on **first-line and subsequent therapies for advanced HCC** in the community setting and impact on patient management were obtained

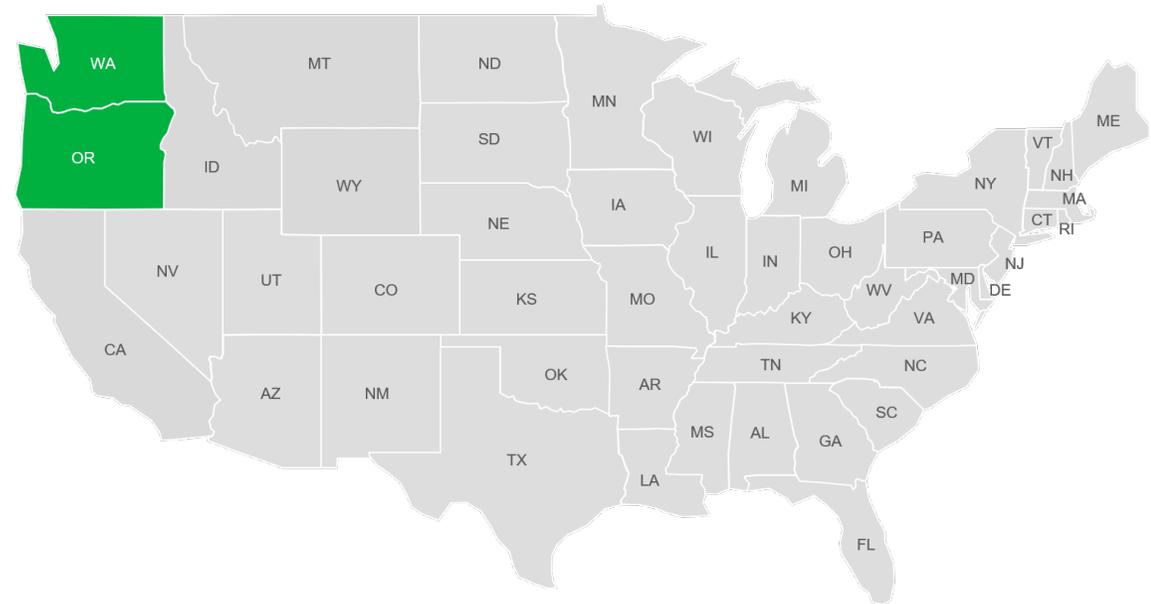
Data collection was accomplished through use of audience response system (ARS) questioning and in-depth moderated discussion

REPORT SNAPSHOT: ATTENDEE OVERVIEW



- > The group of advisors comprised 9 community oncologists from the Pacific Northwest region of the United States
 - Attendees of the roundtable represented community oncologists from Washington and Oregon

INSTITUTION	CITY	STATE
North Star Lodge, Yakima Valley Memorial	Yakima	WA
Virginia Mason Medical Center	Federal Way	WA
UW Medicine-Valley Medical Center	Renton	WA
Compass Oncology	Portland	OR
Swedish Cancer Institute	Issaquah	WA
Swedish Cancer Institute	Seattle	WA
Washington Permanente Medical Group	Tacoma, Silverdale	WA
Providence Regional Cancer Partnership	Everett	WA
Vancouver Clinic	Vancouver	WA



REPORT SNAPSHOT: AGENDA



Time (EST)	Topic
6.00 PM – 6.15 PM (15 min)	Introduction and ARS Questions <ul style="list-style-type: none">• Program overview• Round-robin introductions• ARS questions
6.15 PM – 7.10 PM (55 min)	First-Line Treatment in Advanced HCC <ul style="list-style-type: none">• Overview of current data: Factors guiding first-line therapy<ul style="list-style-type: none">– Sorafenib vs lenvatinib– Incorporation of checkpoint inhibitors<ul style="list-style-type: none">▪ Atezolizumab▪ Nivolumab• Reaction and discussion
7.10 PM – 8.45 PM (95 min)	Second-Line and Subsequent Therapy for Advanced HCC <ul style="list-style-type: none">• ARS questions• Overview of current data<ul style="list-style-type: none">– Subsequent-line therapy<ul style="list-style-type: none">▪ Cabozantinib▪ Nivolumab vs pembrolizumab▪ Ramucirumab (high AFP)▪ Regorafenib▪ Ipilimumab + nivolumab▪ Pembrolizumab• Reaction and discussion
8.45 PM – 9:00 PM (15 min)	Key Takeaways and Meeting Evaluation



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Topline Takeaways and Strategic Recommendations

INSIGHTS INTO HCC

MEETING OBJECTIVES WERE ACHIEVED: TOPLINE TAKEAWAYS



OBJECTIVE

PROCESS

INSIGHTS

[Faded text describing objectives]

[Faded text describing process]

[Faded text describing insights]



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**Key Insights and
Discussion Summary**

KEY INSIGHTS: FIRST-LINE TREATMENT OF ADVANCED HCC (1/2)



How and when is MRD assessed by community oncologists, and does it impact use of immunotherapy in the frontline setting?

MRD is mainly assessed at complete response (CR) by either molecular PCR, MRD or multicolor flow. Immunotherapy is used to treat MRD+ patients in the frontline by about half of the addressors (50%)

- MRD is assessed at CR by half of addressors (50%). The other reports assess MRD at CR and 3 months from induction, and every 3 months thereafter (20%). Only a few reports (10%) assess MRD monthly
 - The time interval approach is performed either by the pathologists in the hospital centers, or by the addressors themselves, depending on the hospital
 - Most of the addressors were aware of the importance of sending the first sample of tumor response approach for MRD assessment
- MRD assessment methods mainly used by the addressors are molecular PCR (20%), and MRD (20%). The multicolor flow is used by 20% of addressors
 - Although MRD is considered more precise in detecting MRD when compared with PCR, its use is limited by the cost, which is considered still too expensive by most addressors
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation
 - However, at least 3 addressors are using immunotherapy to induce MRD negatively after induction (1 addressor in the consolidation of addressors). The remaining addressors would refer their patients to hospital departments

KEY INSIGHTS: FIRST-LINE TREATMENT OF ADVANCED HCC (2/2)



How and when is MRG assessed by community oncologists, and does it impact use of immunotherapy in the frontline setting?

MRG is mainly assessed at complete response (CR) by either molecular PD-L1, MRG or molecular flow. Immunotherapy is used to treat MRG+ patients in the frontline by about half of the addressors (50%).

- MRG is assessed at CR by half of addressors (50%). The other reports assess MRG at CR and 3 months from induction, and every 3 months thereafter (20%). Only a few reports (10%) assess MRG monthly.
 - The time response approach is performed either by the pathologists in the transplant centers, or by the addressors themselves, depending on the hospital.
 - Most of the addressors were aware of the importance of sending the first sample of time response approach for MRG assessment.
- MRG assessment methods mainly used by the addressors are molecular PD-L1 (20%), and MRG (20%). The molecular flow is used by 20% of addressors.
 - Although MRG is considered more precise in detecting MRG when compared with PD-L1, its use is limited by the cost, which is considered still too expensive by most addressors.
- Generally, when patients are MRG+ following induction, the induction therapy is continued, followed by consolidation.
 - However, at least 3 addressors are using immunotherapy to induce MRG negatively after induction (1 addressor is after consolidation of addressors). The remaining addressors would refer their patients to transplant departments.

FIRST-LINE TREATMENT – INSIGHTS AND DATA

"I have not yet used this combination, but I think it is going to be a huge tool for my practice in the future."

1. Treatment success in frontline HCC

Overall survival data was presented. This is an important metric for a cancer therapy, as we want overall survival to be significantly improved compared to standard of care. In this case, the combination of PD-1 and CTLA-4 inhibitors showed a significant improvement in overall survival compared to standard of care. This is a promising result, especially given the high toxicity associated with these treatments. The combination of PD-1 and CTLA-4 inhibitors is a promising approach for the treatment of advanced HCC, and we should continue to explore this combination in future studies.

2. Data needed to confirm front-line HCC in practice

There are a lot of things that need to be considered when evaluating a new combination therapy. In addition to overall survival, we need to consider quality of life, toxicity, and the ability to be used in a wide range of patients. The combination of PD-1 and CTLA-4 inhibitors is a promising approach, but we need to ensure that it is safe and effective in a wide range of patients. We also need to consider the cost of these treatments, as they can be quite expensive. Overall, the combination of PD-1 and CTLA-4 inhibitors is a promising approach for the treatment of advanced HCC, but we need to ensure that it is safe and effective in a wide range of patients.

KEY INSIGHTS: SECOND-LINE AND SUBSEQUENT THERAPY IN TREATMENT OF ADVANCED HCC



How and when is MRG assessed by community oncologists, and does it impact use of immunotherapy in the frontline setting?

MRG is mostly assessed at complete response (CR) by either radiologic (73%), MRG or radiologic free. Immunotherapy is used to treat MRG+ patients in the frontline by about half of the addressors (48%).

- MRG is assessed at CR by half of addressors (48%). The other reports assess MRG at CR and 2 months from induction, and every 2 months thereafter (48%). Only a few reports (11%) assess MRG monthly.
 - The basic response approach is performed either by the pathologists in the management centers, or by the addressors themselves, depending on the hospital.
 - None of the addressors were aware of the importance of sending the first sample of basic response approach for MRG assessment.
- MRG assessment methods mostly used by the addressors are radiologic (73%) and MRG (28%). The radiologic free is used by 20% of addressors.
 - Although MRG is considered more precise in detecting MRG when compared with (73%), its use is limited by the cost, which is considered not too expensive by most addressors.
- Generally, when patients are MRG+ following induction, the induction therapy is extended, followed by consolidation.
 - However, at least 3 addressors are using immunotherapy to induce MRG negatively after induction (1 addressor) or after consolidation (2 addressors). The remaining addressors would refer their patients to management departments.

KEY INSIGHTS: SECOND-LINE AND SUBSEQUENT THERAPY IN TREATMENT OF ADVANCED HCC



How and when is MRG assessed by community oncologists and does it impact use of immunotherapy in the frontline setting?

MRG is mainly assessed at complete response (CR) by either molecular PCR, MRG or multicolor flow. Immunotherapy is used to treat MRG+ patients in the frontline by about half of the advanced HCC.

- MRG is assessed at CR by half of advanced HCCs. The other reports assess MRG at CR and 2 months from induction, and every 2 months thereafter (20%). Only a few reports (17%) assess MRG monthly.
 - The best response approach is performed either by the pathologists in the treatment centers, or by the patients themselves, depending on the facility.
 - Most of the patients were aware of the importance of sending the first sample of best response approach for MRG assessment.
- MRG assessment methods mainly used by the patients are molecular PCR (20%) and MRG (20%). The multicolor flow is used by 20% of patients.
 - Although MRG is considered more precise in detecting MRG when compared with PCR, its use is limited by the cost, which is considered still too expensive by most patients.
- Generally, when patients are MRG+ following induction, the induction therapy is extended, followed by consolidation.
 - However, at least 3 patients are using immunotherapy to induce MRG negatively after induction or after consolidation of patients. The remaining patients would refer their patients to treatment departments.

DISCUSSION: SECOND-LINE AND SUBSEQUENT THERAPY IN ADVANCED HCC (1/2)



SECOND-LINE AND SUBSEQUENT TREATMENT – INSIGHTS AND DATA

“Radiographic progression is, in my mind, the gold standard. Tumor marker progression is also a reference.”

1. Treatment outcomes in Sorafenib (SOF) vs Placebo

The overall survival benefit was modest. This is not necessarily surprising given the complex disease. In our head-to-head comparison, we saw a significant improvement in overall survival with SOF vs placebo, and we would like to see a head-to-head comparison with the next generation of TKIs, and I would like to see the disease-free rate at 1 year. I believe we have not a head-to-head trial of significant benefit with the treatment, and would bring that comparison forward.

2. Data needed to confirm that SOF is beneficial

There are a lot of things that have been done, nothing is better than a RCT and there is no study better with two RCTs together for us either. I would like a SOF study. I would like to see one of the first lines to show benefit in SOF vs something like that. I want something that's clear and that will be more than SOF vs placebo. If the benefits are not very modest, I think a head-to-head of SOF vs placebo would be something that I would be looking at. I would like to see that. There are a lot of things that we can do to help us move forward. In our head-to-head trial, there was a clear benefit with SOF vs placebo, and we would like to see some comparison of efficacy. So, I do think that a lot of things that we can do to help us move forward. I think we're going to start doing the work of the region. SOF is not sufficient.

DISCUSSION: SECOND-LINE AND SUBSEQUENT THERAPY IN ADVANCED HCC (2/2)



SECOND-LINE AND SUBSEQUENT TREATMENT – INSIGHTS AND DATA

“Overall survival is number 1, progression-free survival is number 2. The side effects profile would be my number 3.”

<p>1. Treatment outcomes in patients 18-74.</p>	<p>Overall survival (OS) was the most important outcome. This is not necessarily obvious. OS is a composite outcome, so we have overall survival, progression-free survival (PFS), and overall survival (OS). OS is the most important outcome. OS is the most important outcome. OS is the most important outcome.</p>
<p>2. Data needed to inform your HCC in practice.</p>	<p>OS is the most important outcome. OS is the most important outcome.</p>



Advisor Key Takeaways



ADVISOR KEY TAKEAWAYS (1/2)



ADVISOR

ADVISOR

> The network analysis provided here showed me why it makes a

- There is a better understanding of sequencing therapy
- I really want to talk further with professional and educational but not have a better understanding of those things and have a better idea of when to use them in my practice

- There is a better understanding of some of my other options
- It's particularly interested in the educational and how that will and how would be considered to a secondary option for my own clinical practice
- There's a lot more information to support things and to things the professional that may offer some other options

- It was good to hear about innovations and what's coming down the pipeline for interventional therapy

- There's a lot of good options for around the time just (L2017) and management with device with other people and good response rate
- Responder is an issue

- The interventional therapy, adding the need to have different options besides L2017 and what is going to (L2017)

- It's hoping that some of these interventional agents will get added into practice and hopefully improve the look up

- It's interesting to learn about all these interventional treatments, especially the specific evidence
- It's a lot of options coming up in the future. The only issue will be to learn how to sequence these things

- Not focused on the standard

ADVISOR KEY TAKEAWAYS (2/2)



ADVISOR

ADVISOR

> This is a very troublesome disease, and the winner is clear for

- There is a better understanding of respiratory therapy
- There is a better understanding of the role of the respiratory therapist in the hospital and in the community
- There is a better understanding of the role of the respiratory therapist in the long-term care facility

- There is a better understanding of the role of the respiratory therapist in the hospital and in the community
- There is a better understanding of the role of the respiratory therapist in the long-term care facility
- There is a better understanding of the role of the respiratory therapist in the home care setting

- It was good to hear about innovations and what is coming down the pipeline for respiratory therapy

- There is a lot of good options for around the clock care for COPD and management with device care other people and good response rate
- Respiratory is an issue



- The respiratory therapist is the one to have the most options available for COPD and what is going to come next



- It is hoped that some of these respiratory agents will get added into practice and hopefully improve the outcomes



- It is interesting to learn about all these respiratory treatments, especially the respiratory therapists
- It is an option coming up in the future. The only issue will be to learn how to improve these drugs



- The respiratory therapist is the standard



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INSIGHTS INTO HEPATOCELLULAR CARCINOMA

**ARS RESULTS: FIRST-LINE TREATMENT OF
ADVANCED HCC**

MOST ADVISORS' PATIENT POPULATION COMPRISES 4%–10% OF PATIENTS WITH ADVANCED OR UNRESECTABLE HCC (N = 9)

Approximately what percentage of your patients have advanced/unresectable HCC?

FOR EXAMPLE PURPOSES ONLY

MOST ADVISORS PREFER THE COMBINATION OF ATEZOLIZUMAB AND BEVACIZUMAB AS FIRST-LINE THERAPY FOR UNRESECTABLE HCC (N = 9)

In general, my preferred first-line systemic therapy for unresectable HCC is:

FOR EXAMPLE PURPOSES ONLY

ADVISORS CITE PROVEN EFFICACY AS THE MAIN DRIVER OF FIRST-LINE THERAPY SELECTION (N = 9)

My first-line therapy selection for unresectable HCC is mainly driven by:

FOR EXAMPLE PURPOSES ONLY

THE MAJORITY OF ADVISORS HAVE EXPERIENCE WITH ATEZOLIZUMAB + BEVACIZUMAB IN THE FIRST-LINE SETTING (N = 9)

In how many advanced HCC patients have you ever used atezolizumab + bevacizumab in the first-line setting?

FOR EXAMPLE PURPOSES ONLY

CASE 1

- > A 68-year-old man whose past medical history is significant only for diabetes

- [Blurred text]

MOST ADVISORS WOULD RECOMMEND ATEZOLIZUMAB + BEVACIZUMAB AS FIRST-LINE TREATMENT FOR THIS PATIENT (N = 9)

What would you recommend for this patient?

FOR EXAMPLE PURPOSES ONLY



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**INSIGHTS INTO
HEPATOCELLULAR CARCINOMA**

ARS RESULTS: SECOND-LINE AND
SUBSEQUENT THERAPY FOR ADVANCED
HCC

PREFERRED SECOND-LINE THERAPY VARIED GREATLY AMONG ADVISORS (N = 9)

In general, my preferred second-line therapy for unresectable HCC is:

FOR EXAMPLE PURPOSES ONLY

PROVEN EFFICACY AS SECOND-LINE THERAPY WAS CITED AS THE MAIN DRIVER FOR SELECTION (N = 9)

My second-line therapy selection for unresectable HCC is mainly driven by:

FOR EXAMPLE PURPOSES ONLY

> A 41-year-old white male presents with chronic HBV infection. His

[Blurred text block]

[Blurred text block]

MOST ADVISORS WOULD RECOMMEND CABOZANTINIB AS THE NEXT LINE OF THERAPY FOR THIS PATIENT (N = 9)

What would you recommend for this patient now?

FOR EXAMPLE PURPOSES ONLY

ALL ADVISORS CONSIDER AFP SOMEWHAT IMPORTANT WHEN DETERMINING SECOND-LINE THERAPY (N = 9)

How important is AFP level when determining second-line therapy for your HCC patients?

FOR EXAMPLE PURPOSES ONLY

MOST ADVISORS HAVE USED RAMUCIRUMAB AS SECOND-LINE THERAPY IN PATIENTS WITH UNRESECTABLE HCC (N = 9)



In how many unresectable HCC patients have you ever used the drug ramucirumab in the second-line setting?

FOR EXAMPLE PURPOSES ONLY



ALL ADVISORS HAVE USED CABOZANTINIB AS SECOND-LINE THERAPY IN PATIENTS WITH UNRESECTABLE HCC (N = 9)

In how many unresectable HCC patients have you ever used the drug cabozantinib in the second-line setting?

FOR EXAMPLE PURPOSES ONLY