APTITUDE HEALTH®

CASES

INSIGHTS INTO HEPATOCELLULAR CARCINOMA

Virtual Platform

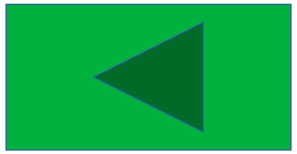
March 15, 2021

Insights From Community Oncologists From the Pacific Northwest, USA

HOW TO NAVIGATE THIS REPORT

CASES

Click to move to topic of interest or ARS supporting data



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Advisor Key Takeaways	
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REPORT OBJECTIVES

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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

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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

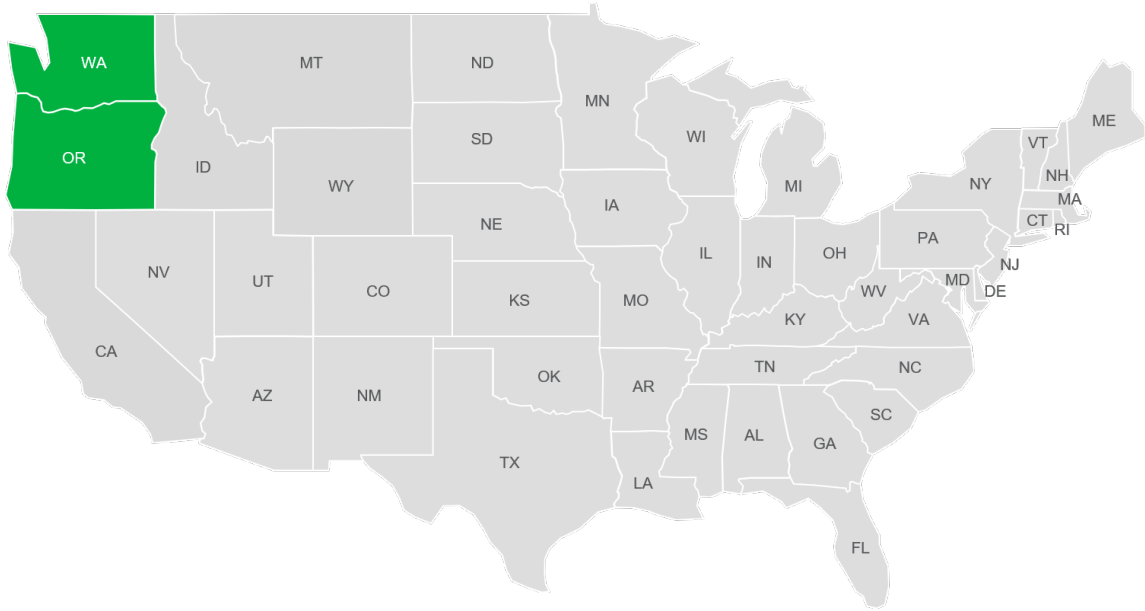
Insights on **first-line and subsequent therapies for advanced HCC** in the community setting and impact on patient management were obtained

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 • Program overview • Round-robin introductions • ARS questions
6.15 PM – 7.10 PM (55 min)	First-Line Treatment in Advanced HCC • Overview of current data: Factors guiding first-line therapy – Sorafenib vs lenvatinib – Incorporation of checkpoint inhibitors ▪ Atezolizumab ▪ Nivolumab • Reaction and discussion
7.10 PM – 8.45 PM (95 min)	Second-Line and Subsequent Therapy for Advanced HCC • ARS questions • Overview of current data – Subsequent-line therapy ▪ 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

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OBJECTIVE

- Understand physicians' expectations for clinical trial data before trying a new regimen in frontline for DLBCL
- Gain insights into R/R patient referral patterns between academic and community practices
- Assess the perception of polatuzumab in the R/R setting compared with other therapeutics (especially CAR T therapy and tafasitamab), including therapy selection and sequencing

PROCESS

Through ARS questions and moderated discussions, community oncologists described their testing practices and challenges they experience

INSIGHTS

- Advisors are open to trying new regimens, primarily with good OS benefit data in frontline, with some open to adopting new therapy with good hazard ratio (0.80 or better) or EFS
- Advisors in community practice typically treat older, less mobile, transplant-ineligible patients and refer out young, fit, transplant-eligible patients
- All advisors generally have positive opinions/experiences with polatuzumab in terms of efficacy and tolerability; however, some currently use it only as a bridge to CAR T, and some in patients ineligible for CAR T. All advisors are unsure about sequencing therapies

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Key Insights and Discussion Summary

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

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

MRD is mainly assessed at complete response (CR) by either molecular PCR, NGS or multicolor flow. Blinatumomab is used to treat MRD+ patients in the frontline by about half of the advisors (1/2)

- MRD is assessed at CR by half of advisors (50%). The other experts assess MRD at CR and 3 months from induction, and every 3 months thereafter (38%). Only a few experts (13%) assess MRD monthly.
  - The bone marrow aspirate is performed either by the pathologists in the transplant centers, or by the advisors themselves, depending on the hospital
  - None of the advisors were aware of the importance of sending the first sample of bone marrow aspirate for MRD assessment
- MRD assessment methods mostly used by the advisors are molecular PCR (38%) and NGS (38%). The multicolor flow is used by 25% of advisors.
  - Although NGS 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 advisors
- Generally, when patients are MRD+ following induction, the induction therapy is extended, followed by consolidation
  - However, at least 3 advisors are using blinatumomab to induce MRD negativity after induction (1 advisor) or after consolidation (2 advisors). The remaining advisors would refer their patients to transplant departments

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

CASES

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DISCUSSION: FIRST-LINE TREATMENT OF ADVANCED HCC (1/3)

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FIRST-LINE TREATMENT – INSIGHTS AND DATA

"For HCC it is always a merging of both the liver function as well as the extent of disease. It really comes down to the best

- [illegible]

- [illegible]

DISCUSSION: FIRST-LINE TREATMENT OF ADVANCED HCC (2/3)

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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."

- Treatment success in frontline (N,BC)

- Data needed to switch from SOC in frontline

DISCUSSION: FIRST-LINE TREATMENT OF ADVANCED HCC (3/3)

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FIRST-LINE TREATMENT – INSIGHTS AND DATA

"I think it makes sense to ask the questions that are being asked [in COSMIC-312], because the overall treatment

- [illegible]

[illegible]

- [illegible]

[illegible]

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

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

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

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

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SECOND-LINE AND SUBSEQUENT TREATMENT – INSIGHTS AND DATA

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

- Treatment success in frontline (1L/IO)

- Data needed to switch from SOC in frontline

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

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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."

- [illegible]

[illegible]

- [illegible]

[illegible]

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Advisor Key Takeaways

ADVISOR KEY TAKEAWAYS (1/2)

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ADVISOR		ADVISOR	
1	> I have a better understanding of sequencing therapies > I really wasn't that familiar with polatuzumab and tafasitamab but now I have a better understanding of these drugs and have a better idea of when to use them in my practice	5	> The network analysis provided here showed me why it makes a > For relapsed/refractory patients it's nice to have different options besides R-CD. and auto or going to CAR-T
2	> I have a better understanding of some of my relapse options > I'm particularly interested in the tafasitamab and hope that tafa and Rev would be tolerated for a second-line option for my very elderly patients > There's a lot more enthusiasm for targeted therapy and for things like polatuzumab that may offer lesser side effects	6	> I'm hoping that some of these second-line agents will get added onto frontline and hopefully improve the cure rate
3	> It was great to hear about innovations and what's coming down the pipeline for relapsed/refractory	7	> Very interesting to learn about all these relapsed/refractory treatments, specifically the bispecific antibodies > A lot of options coming up in the future. The only issue will be to learn how to sequence these drugs
4	> There's a lot of good options for second line than just CAR-T and transplant with decent side effect profile and good response rates > Sequencing is an issue	8	> Still R-CHOP is the standard

ADVISOR KEY TAKEAWAYS (2/2)

CASES

ADVISOR		ADVISOR	
1	> I have a better understanding of sequencing therapies > I really wasn't that familiar with polatuzumab and tafasitamab but now I have a better understanding of these drugs and have a better idea of when to use them in my practice	5	> This is a very troublesome disease, and the winner is clear for > For relapsed/refractory patients it's nice to have different options besides R-ICE and auto or going to CAR-T
2	> I have a better understanding of some of my relapse options > I'm particularly interested in the tafasitamab and hope that tafa and Rev would be tolerated for a second-line option for my very elderly patients > There's a lot more enthusiasm for targeted therapy and for things like polatuzumab that may offer lesser side effects	6	> I'm hoping that some of these second-line agents will get added onto frontline and hopefully improve the cure rate
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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)

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

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

CASES

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

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:

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

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

CASE 1

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

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

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What would you recommend for this patient?

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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)

CASES

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

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

CASES

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

CASE 2

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

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

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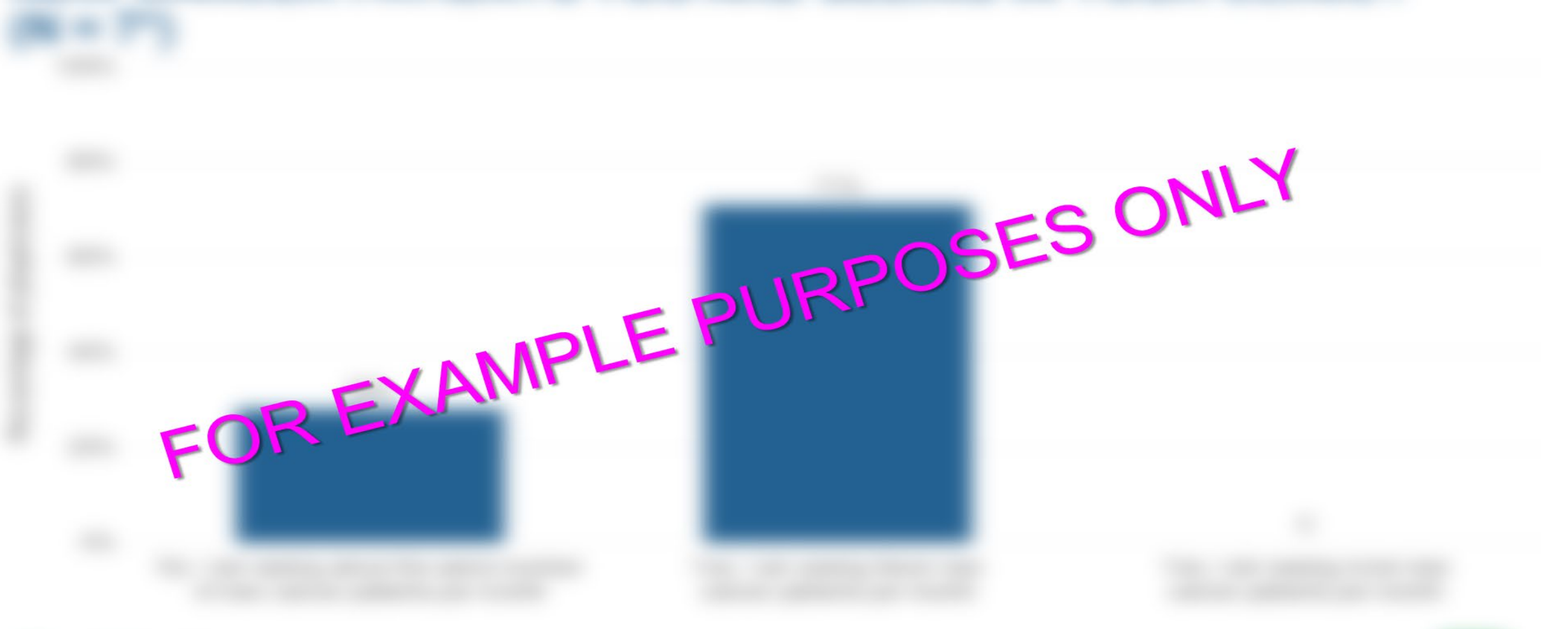
What would you recommend for this patient now?

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?



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

CASES

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

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

CASES

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