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INSIGHTS INTO RENAL CELL CARCINOMA

Virtual Platform

May 5, 2021

Insights From Community Oncologists From the Southeast United States

HOW TO NAVIGATE THIS REPORT

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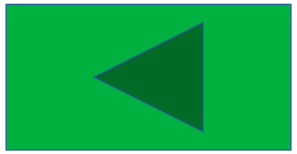
Click to move to topic of interest or ARS supporting data



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REPORT OBJECTIVES

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STUDY OBJECTIVES

To gain advisors' perspectives on

- Current treatment practices regarding therapy of advanced RCC
- 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 Southeast United States in a virtual setting on **May 5, 2021**

Disease state and data presentations were led by **Dr Tian Zhang** from Duke University and moderated by **Dr Sushil Bhardwaj** from the Good Samaritan Regional Medical Center, in conjunction with content developed by the Aptitude Health clinical team

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

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

REPORT SNAPSHOT: ATTENDEE OVERVIEW

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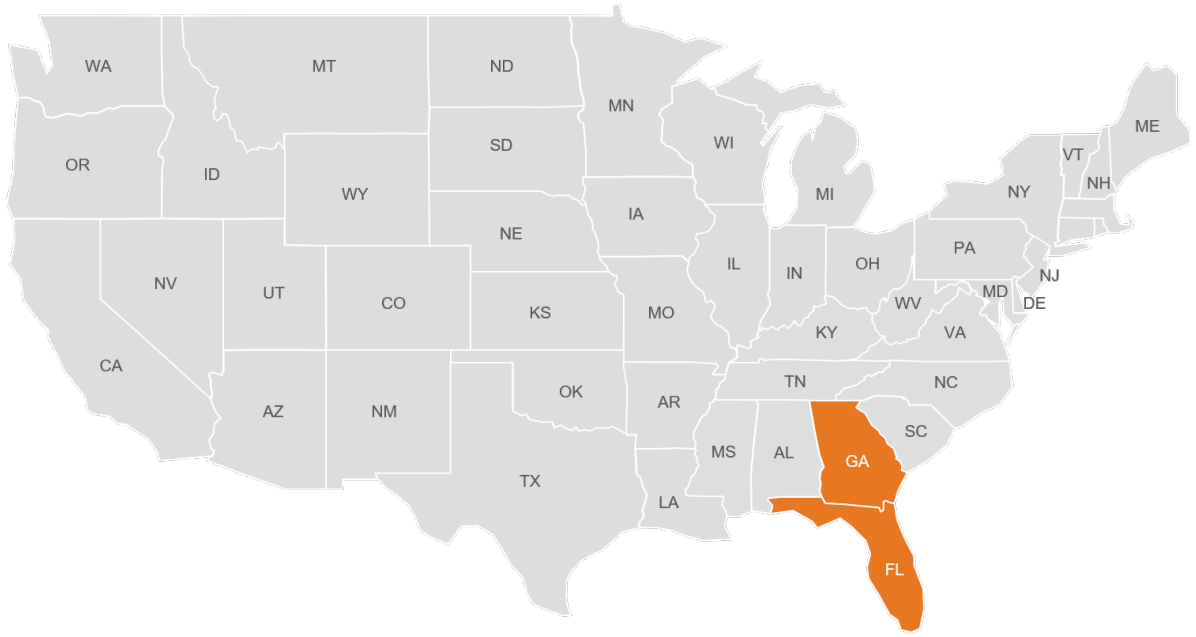
- The group of advisors comprised 9 community oncologists from the Southeast United States
  - Attendees of the roundtable represented community oncologists from Florida and Georgia

INSTITUTION	CITY	STATE
Florida Cancer Specialists	Orlando	FL
Florida Cancer Specialists	Fleming Island	FL
Florida Cancer Specialists	New Port Richey	FL
Florida Cancer Specialists	Lake Worth	FL
Georgia Cancer Specialists	Athens	GA
Georgia Cancer Specialists	Atlanta	GA
Georgia Cancer Specialists	Macon	GA
Georgia Cancer Specialists	Douglasville	GA
Georgia Cancer Specialists	Austell	GA



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 – 7.25 PM (70 min)	**First-Line Therapy in Advanced RCC** • Overview of current data – Selection of approved TKI therapy – Immunotherapy combinations – Review of differential efficacy, safety, and tolerability across TKIs – Cabozantinib in first- vs subsequent-line treatment – Therapy for patients with poor-risk features vs favorable • Reaction and discussion
7.25 PM – 7.35 PM (10 min)	**Break**
7.35 PM – 8.45 PM (70 min)	**Subsequent Management for Advanced RCC** • ARS questions • Overview of current data – Impact of first-line therapy on subsequent therapy sequencing – Therapy following initial TKI failure – TKIs vs immunotherapy vs mTOR inhibition (or combinations?) • 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 RCC

MEETING OBJECTIVES WERE ACHIEVED: TOPLINE TAKEAWAYS (1/2)

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OBJECTIVE	PROCESS	INSIGHTS
• 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	Through AIRS questions and moderated discussions, community oncologists described their testing practices and challenges they experience	• 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 ORR • 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

MEETING OBJECTIVES WERE ACHIEVED: TOPLINE TAKEAWAYS (2/2)

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OBJECTIVE	PROCESS	INSIGHTS
[redacted]	[redacted]	[redacted]

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Key Insights and Discussion Summary

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

CASES

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

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FIRST-LINE TREATMENT – INSIGHTS AND DATA

"I look at the [IMDC] certification for sure, because I think that's going to determine how soon I want to get

- [illegible]

[illegible]

- [illegible]

[illegible]

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

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FIRST-LINE TREATMENT – INSIGHTS AND DATA

"I definitely follow the IDMC risk criteria in determining what kind of first-line treatment the patient needs. But in

- Treatment success in frontline (N,IMC)

- Data needed to switch from ICIC in frontline

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

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FIRST-LINE TREATMENT – INSIGHTS AND DATA

"I think the new [cabo-nivo or pembro-lenvatinib] data just muddies the waters a bit for me. We have a lot more options.

- Treatment success in frontline (IL/RC)

- Data needed to switch from SOC in frontline

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Key Insights: Treatment of Advanced Renal Cell Carcinoma

SUBSEQUENT MANAGMENT FOR ADVANCED RCC

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?

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

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DISCUSSION: SUBSEQUENT MANAGEMENT IN ADVANCED RCC (1/2)

SUBSEQUENT TREATMENT – INSIGHTS AND DATA

"I have certainly had patients that I have just watched for years. They have very indolent, very slow

- [illegible]

- [illegible]

DISCUSSION: SUBSEQUENT MANAGEMENT IN ADVANCED RCC (2/2)

SUBSEQUENT TREATMENT – INSIGHTS AND DATA

"I may try IO-IO following cabo + nivo frontline, especially with the [results of the] JCO trial."

- [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 pancreatic mets data I thought was very interesting. I'm > 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
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)

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ADVISOR		ADVISOR	
	> I felt that the information about the sarcomatoid differentiation,		> One of the things that I really found interesting was the
1	[illegible]	5	[illegible]
2	[illegible]	6	[illegible]
3	[illegible]	7	[illegible]
4	[illegible]	8	[illegible]

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INSIGHTS INTO RENAL CELL CARCINOMA

ARS RESULTS: FIRST-LINE TREATMENT OF ADVANCED RCC

ADVISORS REPORTED USING SINGLE-AGENT TKI TO TREAT RCC PATIENTS WITHIN THE PAST YEAR (N = 6)

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In the past year, in how many unique RCC patients have you used a single-agent TKI inhibitor?

*Three advisors did not respond.

ADVISORS HAVE EXPERIENCE USING CABOZANTINIB AS FIRST- OR SUBSEQUENT-LINE THERAPY FOR ADVANCED RCC (N = 6)

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In the past year, in how many unique RCC patients have you used the drug cabozantinib?

*Three advisors did not respond.

ADVISORS REPORTED HAVING SOME EXPERIENCE WITH AXITINIB + PEMBROLIZUMAB IN THE PAST YEAR (N = 6)

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In the past year, in how many unique RCC patients have you used axitinib + pembrolizumab?

*Three advisors did not respond.

ADVISORS HAVE EXPERIENCE WITH IPILIMUMAB + NIVOLUMAB IN THE FIRST-LINE SETTING (N = 6)

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In the past year, in how many unique RCC patients have you used ipilimumab + nivolumab?

*Three advisors did not respond.

MOST ADVISORS HAVE NEVER USED THE COMBINATION OF CABOZANTINIB + NIVOLUMAB AS FIRST-LINE THERAPY IN RCC (N = 6)

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In how many unique RCC patients have you used cabozantinib + nivolumab?

*Three advisors did not respond.

ALL ADVISORS AGREE THAT HEPATIC METASTASES CARRY THE WORST PROGNOSIS IN METASTATIC RCC (N = 7)

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Which site of metastasis carries the worst prognosis in metastatic kidney cancer patients?

*Two advisors did not respond.

MOST ADVISORS WERE UNAWARE THAT CABOZANTINIB ALSO TARGETS MET/AXL (N = 7)

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Cabozantinib differs from other VEGFR TKIs in its ability to inhibit which targets?

*Two advisors did not respond.

PATIENT CASE 1

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- A 58-year-old man, diagnosed with RCC 4 years ago, underwent radical

MOST ADVISORS WOULD RECOMMEND AXITINIB + PEMBROLIZUMAB AS FIRST-LINE TREATMENT FOR THIS LOW-RISK PATIENT (N = 6)

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What would you recommend for this patient at this time?

*Three advisors did not respond.

PATIENT CASE 2

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- A 70-year-old man was initially found to have a 6-cm mass in his left kidney with

MOST ADVISORS WOULD USE A TKI + IO THERAPY FOR THIS INTERMEDIATE-RISK PATIENT, SPLIT BETWEEN AXI + PEMBRO OR CABO + NIVO (N = 7)

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What would you recommend for this patient at this time?

*Two advisors did not respond.

PATIENT CASE 3

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- A 68-year-old woman presents with severe fatigue, blood in her urine, and pain in

MOST ADVISORS WOULD RECOMMEND IPILIMUMAB + NIVOLUMAB AS FIRST-LINE TREATMENT FOR THIS HIGH-RISK PATIENT (N = 6)

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What would you recommend for this patient?

*Three advisors did not respond.

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INSIGHTS INTO RENAL CELL CARCINOMA

ARS RESULTS: SUBSEQUENT MANAGEMENT FOR ADVANCED RCC

MOST ADVISORS PREFER CABOZANTINIB AS SECOND-LINE THERAPY FOR ADVANCED RCC (N = 8)

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Which agent(s) do you prescribe most frequently for second-line therapy?

*One advisor did not respond.

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

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

PATIENT CASE 2, CONTINUED

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- The 70-year-old male with past nephrectomy and metastatic RCC (liver and lymph

MOST ADVISORS WOULD RECOMMEND CABOZANTINIB AS THE NEXT LINE OF THERAPY FOR THIS PATIENT (N = 8)

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What would you recommend for this patient now?

*One advisor did not respond.