



# Insights Into Renal Cell Carcinoma

Virtual Platform

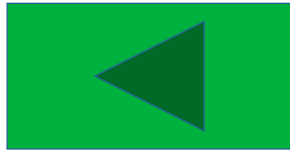
February 23, 2022

Insights From Southwest Community Oncologists

# How to Navigate This Report









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# Report Snapshot: Session Overview



A moderated roundtable discussion was held with oncologists across the Southwest region of the United States in a virtual setting on **February 23, 2022**

Disease state and data presentations were led by **Dr Rana McKay** from UC San Diego 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 and impact on patient management

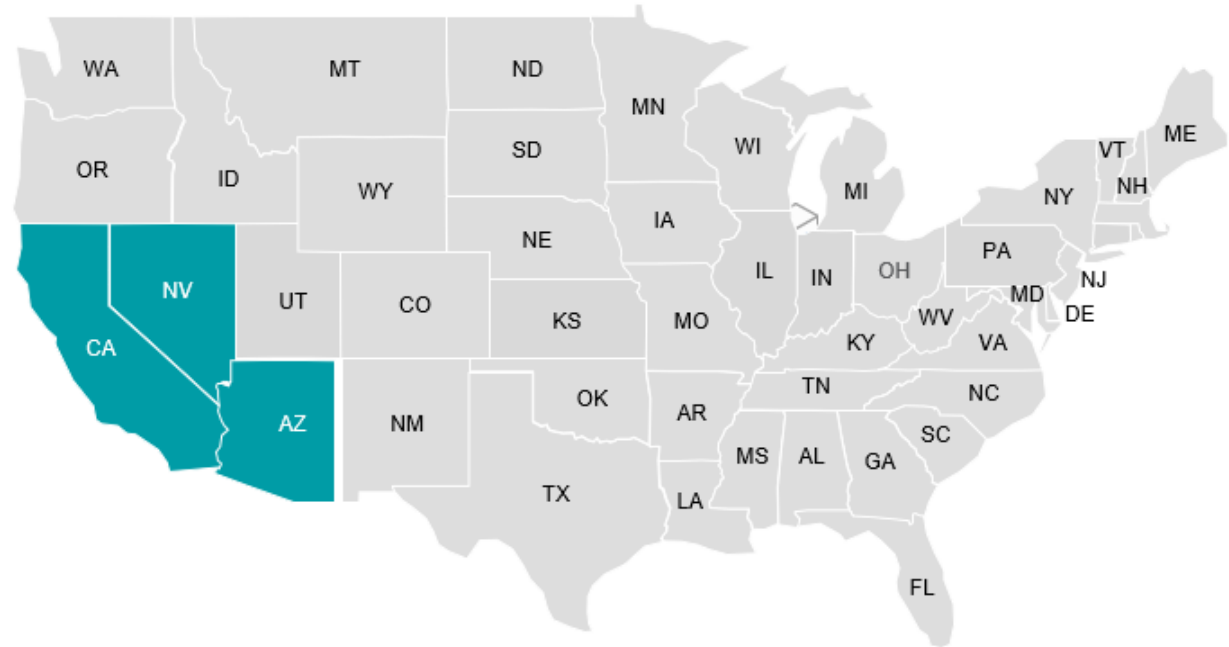
Data collection was accomplished through use of audience response system (ARS) questioning and in-depth moderated discussion

# Report Snapshot: Attendee Overview



- > The group of advisors comprised 10 oncologists from the Southwest region of the United States

INSTITUTION	CITY	STATE
Arizona Center for Cancer Care	Scottsdale	AZ
Desert Hematology Oncology	Surprise	AZ
Comprehensive Cancer Centers of Nevada	Las Vegas	NV
Loma Linda University	Loma Linda	CA
Ventura County Hematology Oncology Specialists	Ventura	CA
Palo Verde Cancer Specialists	Phoenix	AZ
Cancer and Blood Specialty Clinic	Los Alamitos	CA
Ironwood Cancer & Research Centers	Mesa	AZ
Kaiser Permanente	San Diego	CA
Keck Medicine of USC	Huntington Beach	CA



# Report Snapshot: Agenda



Time (ET)	Topic
6.00 PM – 6.15 PM (15 min)	<b>Introduction and ARS Questions</b> <ul style="list-style-type: none"><li>• Program overview</li><li>• Introductions</li><li>• ARS questions</li></ul>
6.15 PM – 7.25 PM (70 min)	<b>First-Line Therapy in Advanced RCC</b> <ul style="list-style-type: none"><li>• Overview of current data</li><li>• Reaction and discussion</li></ul>
7.25 PM – 7.35 PM (10 min)	<b>Break</b>
7.35 PM – 8.45 PM (70 min)	<b>Subsequent Management for Advanced RCC</b> <ul style="list-style-type: none"><li>• ARS questions</li><li>• Overview of current data</li><li>• Reaction and discussion</li></ul>
8.45 PM – 9.00 PM (15 min)	<b>Key Takeaways and Meeting Evaluation</b>



# Key Insights and Discussion Summary

## FIRST-LINE TREATMENT – INSIGHTS AND DATA

*“I definitely go by the risk status, high risk, intermediate, and low risk. And so for my low-risk patients, kind of*

1. Treatment success in frontline OS/RRS

“The overall survival that’s what we want. This is not necessarily disease-free or overall survival, so we want overall survival.”  
 “I would not use a treatment approach with that using ICI or mTOR, and I would not start the disease-free rate at 1 year. I believe in that ICI is important there is significant benefit with the treatment, and overall going from something like 18 months.”

2. Data needed to switch from ICI to frontline

“One of all a lot of things have been that, getting a better than 18 months and maybe 18 months, maybe with that 18 months, getting to the overall.”  
 “I would not use a treatment approach with that using ICI or mTOR, and I would not start the disease-free rate at 1 year. I believe in that ICI is important there is significant benefit with the treatment, and overall going from something like 18 months.”  
 “The overall survival rate, that’s what we want. This is not necessarily disease-free or overall survival, so we want overall survival.”  
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## FIRST-LINE TREATMENT – INSIGHTS AND DATA

*“I have [used cabozantinib] in combination but not as a single agent.”*

1. Treatment success in frontline mRCC

The overall survival benefit was not seen. This is not unexpected because this is a complex disease, so we need overall survival. I would not see significant long-term benefit. I think when I define success, I would define it as a treatment approach either that using VEGF or mTOR, and I would say either the disease-free rate or I would say overall OS as a measure of there is significant benefit with the treatment, and overall being that something is achievable.

2. Data needed to justify front-line use of cabozantinib

One of the main things that have been done, nothing is better than Axitinib and Nivolumab. It would be hard to see how Axitinib performs for the patients. I would be a little skeptical. I would not be one of the first ones to move toward mTOR or something like that. I want something that's been done and we know how well it works. If the benefits are not very obvious, then a higher rate of OS or better overall something that I would be looking at. Overall survival data, that's what we're looking for. OS is a hard-to-achieve, so you do have to see some surrogate of efficacy. So, I do think that a lot of people would be surprised that we're going to start doing the use of any agent. OS is what matters.

## FIRST-LINE TREATMENT – INSIGHTS AND DATA

*“I think most of my patients can tolerate axitinib + pembro frontline. I’ve used that quite a bit. And then my*

1. Treatment success in frontline (3/4)

The overall survival benefit was seen. This is not necessarily disease-free or overall survival, so we need overall survival. I think there are significant long-term benefits. I think when you have a disease, you can have a treatment approach with that using PD-1 or PD-L1, and I think we should be looking at that as a long-term benefit. I think there is a significant benefit with the treatment, and we should be looking at that as a long-term benefit.

2. Data needed to justify front-line (3/4)

The overall survival benefit was seen, which is better than the overall survival. I think there are significant long-term benefits. I think when you have a disease, you can have a treatment approach with that using PD-1 or PD-L1, and I think we should be looking at that as a long-term benefit. I think there is a significant benefit with the treatment, and we should be looking at that as a long-term benefit.

## FIRST-LINE TREATMENT – INSIGHTS AND DATA

*"[On CheckMate 9ER data] I mean, it demonstrated statistically significant improvement in overall survival across*

1. Treatment success in frontline (S, 2023)

The overall survival benefit was seen. This is a very important message. This is a positive message. It is not just overall survival. It is also overall survival. I mean, it demonstrated statistically significant improvement in overall survival across all subgroups. I mean, it demonstrated statistically significant improvement in overall survival across all subgroups. I mean, it demonstrated statistically significant improvement in overall survival across all subgroups. I mean, it demonstrated statistically significant improvement in overall survival across all subgroups.

2. Data needed to justify from S, 2023 in frontline

This is all a lot of things have been said. Nothing is better than CheckMate 9ER and S, 2023. It is really hard to see CheckMate 9ER as the winner. I mean, it demonstrated statistically significant improvement in overall survival across all subgroups. I mean, it demonstrated statistically significant improvement in overall survival across all subgroups. I mean, it demonstrated statistically significant improvement in overall survival across all subgroups. I mean, it demonstrated statistically significant improvement in overall survival across all subgroups.



# Key Insights: Treatment of Advanced Renal Cell Carcinoma

Subsequent Management of Advanced RCC

## SUBSEQUENT TREATMENT – INSIGHTS AND DATA

*“I scan them every 3 months with the full-body scans. If the patient has a new mass, of course that’s the clear sign*

### 1. Treatment success in frontline SCLC

The overall survival benefit was not seen. This is not unexpected because this is a highly aggressive disease. In our first cohort survival was not significantly improved compared to placebo. There were no adverse events. I would rather use a treatment approach rather than using 100% of 100% and I would not expect the disease-free rate in 2 years. I believe as there is a significant impact of these 2 significant events with the treatment, and overall being that something is achievable.

### 2. Data needed to confirm from SCLC in frontline

There are a lot of things that have been done, nothing is better than 100% and there is a really high level of 100% patients for the patients. I would be a little bit more. I would not be one of the first ones to move forward on 100% or anything like that. I want something that's not just a number and we know that we can't do it. If the benefits are not very clear, there is a need for 100% or better would be something that I would be looking at. There's survival data, that's what we're looking at. It's a hard to come by, so you do have to use some surrogate of efficacy. So, I do think that it is a hard surrogate because even if you have a high survival rate, it's not going to be the end of the line. 100% is not sufficient.

## SUBSEQUENT TREATMENT – INSIGHTS AND DATA

*“I think lenvatinib is very effective, but the dose is a little bit something that I get hesitant.”*

1. Treatment success in frontline (N=202)

The overall survival benefit was seen. This is not necessarily disease-free or quality of life benefit. In our real-world setting, I would not use a treatment approach other than using VEGF or mTOR, and I would not start the disease-free rate at 1 year. I believe that this is a significant finding in significant setting with the treatment, and I would say that something is available.

2. Data needed to confirm from RCC in frontline

That at all, a lot of things have been done, nothing is better than VEGF and mTOR. In early days, with low VEGF inhibitors for my patients, I would be a little hesitant. I would not be one of the first ones to move toward mTOR or something like that. I want something that has been used and we know that it works. If the benefits are not very strong, I think a higher rate of VEGF or mTOR would be something that I would be looking at. Overall survival rate, that's what we're looking at. It's a hard to come by, so you do have to use some surrogate of efficacy. So, I do think that a lot of people would be looking at that, or that, which is going to start during the use of any agent. VEGF or mTOR inhibitors.

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## SUBSEQUENT TREATMENT – INSIGHTS AND DATA

### General comments:

*“My go-to combination is the pembro + axi and cabo + nivo.”*

1. Treatment success in frontline (2022)

The overall survival benefit was not clear. This is not necessarily because there is no benefit, but because overall survival is a very noisy endpoint. In the pembro + axi vs placebo + axi comparison, the overall survival benefit was not clear. In the cabo + nivo vs placebo + nivo comparison, the overall survival benefit was not clear. In the pembro + axi + cabo vs placebo + axi + cabo comparison, the overall survival benefit was not clear. In the pembro + axi + cabo + nivo vs placebo + axi + cabo + nivo comparison, the overall survival benefit was not clear.

2. Data needed to confirm front-line (2022) vs frontline

There are a lot of things that have been done, nothing is better than pembro + axi + cabo + nivo. In the pembro + axi + cabo + nivo vs placebo + axi + cabo + nivo comparison, the overall survival benefit was not clear. In the pembro + axi + cabo + nivo vs placebo + axi + cabo + nivo comparison, the overall survival benefit was not clear. In the pembro + axi + cabo + nivo vs placebo + axi + cabo + nivo comparison, the overall survival benefit was not clear. In the pembro + axi + cabo + nivo vs placebo + axi + cabo + nivo comparison, the overall survival benefit was not clear.

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## SUBSEQUENT TREATMENT – INSIGHTS AND DATA

After cabo-nivo:

*“If my first line is cabo + nivo, then the available second line is tivo.”*

1. Treatment success in frontline (S,ORR)

The overall survival benefit was seen. This is not necessarily disease-free or overall survival, as we have overall survival. I would not say significant improvement overall. I think when you're comparing, I would rather use a treatment endpoint rather than using OS or ORR, and I would say that the disease-free rate at 1 year is actually as high as 10% compared to what is significant overall with the treatment, and overall doing that comparing overall.

2. Data needed to switch from S,ORR to frontline

That's all a lot of things have been that, nothing is better than S,ORR and maybe, I would rather use that S,ORR endpoint for my patients. I would be a little bit more, I would be a little bit more of the first line to move forward on ORR or something like that. I want something that's not just OS and ORR and OS and ORR and OS. If the benefits are not very strong, I think a hazard ratio of 0.85 or better would be something that I would be looking at. I think overall, that's what, but in this disease, that OS is hard to come by, so you do have to use some surrogate of efficacy. So, I do think that's a bit of a trade-off between overall survival and OS, so that's what's going to start driving the use of any agent. ORR is not sufficient.





## Advisor Key Takeaways

# Advisor Key Takeaways

## ADVISOR

### > Combination therapy (TKI + IO) is promising

- There is a better understanding of sequencing therapy
- I really want that number with combination and sequential but we have a better understanding of those drugs and have a better idea of when to use them in the practice
- There is a better understanding of some of the newer options
- It is particularly important in the adjuvant and high risk sets and there would be interest for a sequential option for the early adjuvant setting
- There is a lot more evidence for targeted therapy and for things like pembrolizumab that may offer some side effects
- It was good to hear about combinations and what's coming down the pipeline for immunotherapy
- There is a lot of good options for adjuvant but that just need to be managed with disease with other profile and good response rates
- Sequencing is an issue

## ADVISOR

### > Data about lenvatinib + pembro and second-line cobimetinib is good

- The immunotherapy setting is not to have different options besides PD-1 and what is going to come?
- We hope that some of these immunotherapy agents will get added into frontline and hopefully improve the look rate
- Very interesting to learn about all these immunotherapy treatments, especially the targeted antibodies
- A lot of options coming up in the future. The only issue will be to learn how to sequence these drugs
- Not to be afraid of the standard



# Insights Into Renal Cell Carcinoma

ARS Results: First-Line Treatment of Advanced RCC

# About 70% of the Advisors Have Used Single-Agent TKI to Treat RCC Patients as a First-Line Therapy in the Past Year (N = 10)

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

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# All Advisors Have Used Axitinib + Pembrolizumab to Treat RCC Patients as a First-Line Therapy in the Past Year (N = 10)

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

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# About 80% of the Advisors Have Used Cabozantinib + Nivolumab as a First-Line Therapy in the Past Year (N = 10)

In how many unique RCC patients have you used cabozantinib + nivolumab as a first-line therapy?

FOR EXAMPLE PURPOSES ONLY



# About 33% of the Advisors Have Used Lenvatinib + Pembrolizumab as a First-Line Therapy in the Past Year (n = 9\*)



In the past year, in how many unique RCC patients have you used lenvatinib + pembrolizumab as a first-line therapy?

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# Only 11% of the Advisors Have Used Axitinib + Avelumab as a First-Line Therapy to Treat RCC Patients in the Past Year (n = 9\*)

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

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# 80% of the Advisors Have Used Ipilimumab + Nivolumab as First-Line Therapy for RCC in the Past Year, but the Majority Have Only Limited Use (N = 10)

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

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# Overall Survival Was Cited as the Main Driver for Selection of First-Line Therapy (N = 10)



When evaluating new options for first-line treatment of RCC, which of the following aspects is the most influential on therapy choice?

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# Half of the Advisors Believe Hepatic Metastases Carry the Worst Prognosis in Metastatic Kidney Cancer Patients (N = 10)



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

60%

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# Patient Case 1

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

*[Blurred text block]*

> *[Blurred text block]*

# Most Advisors Would Recommend IO + TKI (most frequently axi-pembro) as First-Line Treatment for This Low-Risk Patient (N = 10)

What would you recommend for this patient at this time?

FOR EXAMPLE PURPOSES ONLY



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

...

# Most Advisors Would Recommend IO + TKI (nearly half with axi-pembro) as First-Line Treatment for This Intermediate-Risk Patient (n = 9\*)

What would you recommend for this patient at this time?

FOR EXAMPLE PURPOSES ONLY



# Patient Case 2, Continued

> Assume the same 70-year-old man (6-cm mass in his left kidney; clear cell

• [Faded text]



# Half of the Advisors Would Recommend TKI (cabozantinib) as Next-Line Treatment for This Intermediate-Risk Patient (N = 10) Who Previously Received Pembro as Adjuvant Therapy

What would you recommend for this patient in this situation?

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# Patient Case 3



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

the lower back. She reports that the pain is worse in the morning and improves with activity. She also mentions that she has noticed some weight loss over the past few months. Her medical history is significant for hypertension and type 2 diabetes. She is currently on lisinopril and metformin. Her physical examination is unremarkable. Laboratory studies show a hemoglobin of 10.5 g/dL, hematocrit of 31.5%, and a normal urinalysis. Her serum creatinine is 1.2 mg/dL. Her ESR is 45 mm/hr. Her chest X-ray and CT scan of the abdomen are normal. Her bone density scan shows osteopenia. Her rheumatoid factor and ANA are negative. Her ferritin is 150 ng/mL. Her serum iron is 150 µg/dL. Her total iron-binding capacity is 300 µg/dL. Her transferrin saturation is 50%. Her serum calcium is 9.5 mg/dL. Her parathyroid hormone-related protein is 15 pg/mL. Her parathyroid hormone is 100 pg/mL. Her 25-hydroxyvitamin D is 10 ng/mL. Her 1,25-dihydroxyvitamin D is 30 pg/mL. Her prolactin is 15 ng/mL. Her growth hormone is 0.5 µg/L. Her insulin-like growth factor-1 is 0.5 µg/L. Her prolactin is 15 ng/mL. Her growth hormone is 0.5 µg/L. Her insulin-like growth factor-1 is 0.5 µg/L.

Her physical examination is unremarkable. Laboratory studies show a hemoglobin of 10.5 g/dL, hematocrit of 31.5%, and a normal urinalysis. Her serum creatinine is 1.2 mg/dL. Her ESR is 45 mm/hr. Her chest X-ray and CT scan of the abdomen are normal. Her bone density scan shows osteopenia. Her rheumatoid factor and ANA are negative. Her ferritin is 150 ng/mL. Her serum iron is 150 µg/dL. Her total iron-binding capacity is 300 µg/dL. Her transferrin saturation is 50%. Her serum calcium is 9.5 mg/dL. Her parathyroid hormone-related protein is 15 pg/mL. Her parathyroid hormone is 100 pg/mL. Her 25-hydroxyvitamin D is 10 ng/mL. Her 1,25-dihydroxyvitamin D is 30 pg/mL. Her prolactin is 15 ng/mL. Her growth hormone is 0.5 µg/L. Her insulin-like growth factor-1 is 0.5 µg/L.

# Most Advisors Would Recommend IO + TKI (most frequently axi-pembro) as First-Line Treatment for This High-Risk Patient (N = 10)

What would you recommend for this patient at this time?

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# Insights Into Renal Cell Carcinoma

ARS Results: Subsequent Management of Advanced RCC

# The Majority of the Advisors Prefer Cabozantinib as Second-Line Therapy for Advanced RCC (n = 9\*)



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

100%

FOR EXAMPLE PURPOSES ONLY



# Proven Efficacy Was the Most Frequently Cited Driver for Selection of Second-Line Therapy (N = 10)

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

60%

FOR EXAMPLE PURPOSES ONLY



# Patient Case 2, Continued

> The 70-year-old male with past nephrectomy and metastatic RCC (liver and lymph nodes) was initially started on axitinib + pembrolizumab. Eleven months later his

metastatic disease was stable on axitinib + pembrolizumab. He was then started on nivolumab + ipilimumab. His disease was stable on nivolumab + ipilimumab for 11 months. He was then started on nivolumab + ipilimumab + axitinib. His disease was stable on nivolumab + ipilimumab + axitinib for 11 months. He was then started on nivolumab + ipilimumab + axitinib + pembrolizumab. His disease was stable on nivolumab + ipilimumab + axitinib + pembrolizumab for 11 months.

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# Most of the Advisors Would Recommend Cabozantinib as the Next Line of Therapy for This Patient (N = 10)



What would you recommend for this patient now?

80%

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