

Addressing Gaps in Education for Non-Clear Cell RCC



Moshe Ornstein, MD, MA

As part of an *Around the Practice*® program, CancerNetwork hosted a panel discussion on renal cell carcinoma (RCC) to discuss differentiation in the identification and treatment of clear and non-clear cell RCC. The panel also discussed challenges associated with patient education on non-clear cell RCC.

The panel was led by **Moshe Ornstein, MD, MA**, a genitourinary medical oncologist at the Cleveland Clinic. Panelists included **Karine Tawagi, MD**, assistant professor of medicine in the Department of Hematology and Oncology at the University of Illinois College of Medicine; **Mahdi Taha, DO, FACOI, FACP**, hematologist and

medical oncologist at Florida Cancer Specialists; and **Nataliya Mar, MD**, associate professor in the Division of Hematology and Oncology at the University of California Irvine.

Ornstein / In terms of clear cell vs non-clear cell, how do you look at these 2 large categories of RCC and differentiate between them, and what is your general treatment paradigm for these patients?

Tawagi / Most of the kidney cancers that we see are clear cell, about 80%. We know that sarcomatoid dedifferentiation can happen in about 20% of RCCs, regardless of the histology subtype. When we think about non-clear cell

RCC, it is a heterogeneous group of patients. Although they are classically lumped together, treatment-wise ... we cannot lump them all together, although we will dive into some of the trials that do lump them together.

The most common type with a non-clear cell is papillary RCC, which accounts for up to 15% to 20% [of cases]. Previously, it was broken down into type 1 and type 3, but then in 2022, the World Health Organization reclassified them, and we eliminated those subtypes. Historically, type 2 was the more aggressive subtype, but we know that this is a heterogeneous group, so they were reclassified.

For that reason, one of the next most common non-clear cell RCCs that we have is chromophobe RCC, which accounts for up to 10% [of cases]. It can grow more slowly but can be locally invasive. It often has a more intermediate prognosis between clear cell and non-clear cell. Then we have the collecting duct [carcinoma], which falls on the more aggressive spectrum of kidney cancers [and] is [rarer]. We have medullary RCC, which is, again, a rare subtype [and] is often associated with sickle cell disease.

Then there are even [rarer] subtypes. There are mucinous tubular and spindle [RCC], clear cell [RCC], and papillary RCCs. In terms of who is affected with these, we see non-clear cell usually at an older age, and both clear cell and non-clear cell have a slight male predominance.... Risk factors seen with...clear cell, [include] smoking, obesity,

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Nataliya Mar, MD

hypertension, and a family history of kidney cancer. There are also hereditary syndromes that we can check for. Specifically, if somebody presents at a younger age, we think about von Hippel-Lindau [disease] or VHL, tuberous sclerosis, *BAP1*, or Birt-Hogg-Dubé [syndrome]. Then, in non-clear cell, there are also some genetic syndromes that can be associated with some of the subtypes of non-clear cell, and those also impact how we think about treatment.

Ornstein / When seeing a patient who comes in with a diagnosis of non-clear cell, are there specific challenges in taking care of these patients compared with the clear cell population? What [are] the biggest challenges when seeing a patient with non-clear cell RCC?

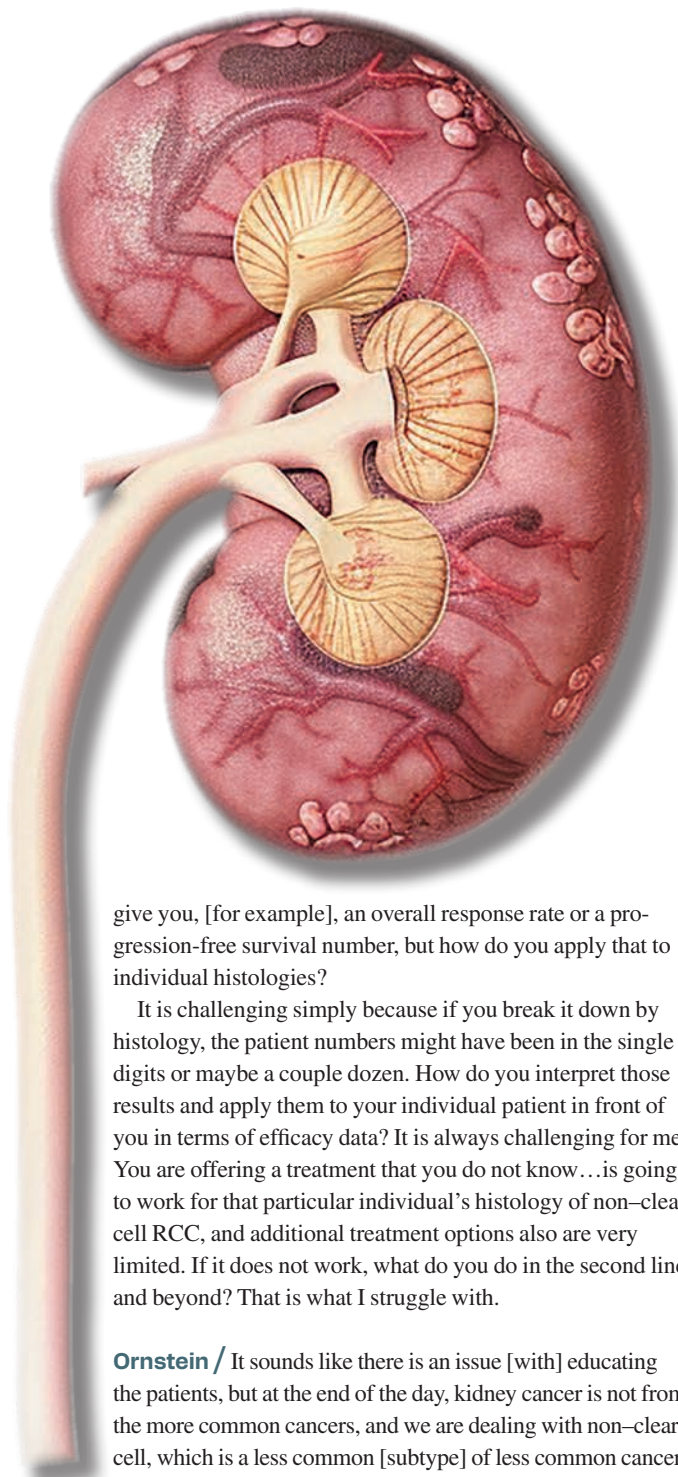
Taha / There are, especially from a non-clear cell perspective, because—and I am speaking from a community practice setting—the [number] of resources that are available for non-clear cell, just as a whole, is significantly limited compared with clear cell. When a patient presents and comes in, usually the information... is associated with clear cell RCC. Then they look to you for guidance, especially from a community oncology perspective.

Because I did come from a national oncology center where I led a genitourinary clinic for 6 years, and I had an abundance of resources, I had genetic counselors, [and] we were able to test for familial syndromes. I had numerous clinical trials available to me... but non-clear cell is significantly [rarer]. I do not have that many resources available for these patients.

We have a good discussion with respect to what [patients'] resources are and what is available to them. Then there is an educational discussion that happens, especially during that initial consult, about how non-clear cell differentiates from clear cell, and what we can do to educate these patients. That is step 1: making them aware that their [prognosis] is a little different than what they are traditionally reading about.

Ornstein / Are the challenges similar in terms of having to educate patients and what resources are available? How do they differentiate in a more traditional academic setting from the patients who are coming in with non-clear cell RCC?

Mar / To build on the previous comment,... patients do look for guidance from their physician. I personally always struggle in terms of how to interpret the previous clinical trial data concerning non-clear cell because, until very recently, the clinical trials have been very small. If all of the different non-clear cell subtypes were put together into 1 trial they



give you, [for example], an overall response rate or a progression-free survival number, but how do you apply that to individual histologies?

It is challenging simply because if you break it down by histology, the patient numbers might have been in the single digits or maybe a couple dozen. How do you interpret those results and apply them to your individual patient in front of you in terms of efficacy data? It is always challenging for me. You are offering a treatment that you do not know... is going to work for that particular individual's histology of non-clear cell RCC, and additional treatment options also are very limited. If it does not work, what do you do in the second line and beyond? That is what I struggle with.

Ornstein / It sounds like there is an issue [with] educating the patients, but at the end of the day, kidney cancer is not from the more common cancers, and we are dealing with non-clear cell, which is a less common [subtype] of less common cancer. Then we are breaking those down into further subtypes, so now we are at single percentages with trials that maybe were broad. We are trying to tease out subgroups from different trials to provide the best treatment option for patients. This demonstrates how much there is a need for education across the board [for] providers and patients, and all sorts of resources that are required, especially with the emerging data. ■