Kidney Cancer Combinations: Tracking and Treating Symptoms With the Challenge of Combination Therapy

PRESENTED BY KATHLEEN BURNS, AGACNP-BC, OCN®

From City of Hope National Medical Center, Duarte, California

Presenter's disclosure of conflicts of interest is found at the end of this article.

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Abstract

At JADPRO Live Virtual 2020, Kathleen Burns, AGACNP-BC, OCN®, discussed strategies to track and treat symptoms associated with combination therapies for the treatment of renal cell carcinoma.

Over the past 10 years, the arrival of immunotherapies and targeted agents has extended the survival and improved the quality of life for patients with renal cell carcinoma (RCC), but these novel therapies have also introduced challenging new side effects.

During JADPRO Live Virtual 2020, Kathleen Burns, AGACNP-BC, OCN®, of City of Hope National Medical Center, discussed strategies to track and treat symptoms associated with combination therapies.

RCC TREATMENT LANDSCAPE

Clear cell RCC, the most prevalent type of RCC, is divided into patients with favorable risks and poor/intermediate risks. These categories are determined by certain characteristics that have prognostic value, such as calcium level, platelet level, neutrophils, hemoglobin, and time from diagnosis to initiation of systemic treatment.

There are currently four combination protocols that are used in RCC:

- Nivolumab (Opdivo, a PD-1 inhibitor)/ipilimumab (Yervoy, a CTLA-4 inhibitor)
- Axitinib (Inlyta, a targeted agent)/avelumab (Bavencio, a PD-L1 inhibitor)
- Axitinib (Inlyta, a targeted agent)/pembrolizumab (Keytruda, a PD-1 inhibitor)
- Cabozantinib (Cabometyx, a targeted agent)/nivolumab (Opdivo, a PD-1 inhibitor)

With immunotherapy, the primary toxicities are related to an overactive immune system against a specific target, and pneumonitis and adrenal insufficiency are both common side effects.

Many of the targeted therapies used in renal cell carcinoma, on the other hand, are VEGF tyrosine kinase inhibitors (TKIs) and have a

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side effect profile that includes hypertension, appetite issues such as anorexia, and cytopenias.

With combination therapies, however, it's necessary to consider overlapping toxicities, said Ms. Burns. Diarrhea, skin changes, and hepatitis are all overlapping toxicities of immunotherapy and targeted therapy (Figure 1).

When educating patients about immunotherapy, Ms. Burns underscored the importance of providing patients with a realistic picture of all potential side effects, even those that occur in only a small number of patients.

"One characteristic of immunotherapy side effects is that they can happen at any time, whether it's the first or the tenth cycle of treatment or even after a drug has been discontinued," said Ms. Burns.

"The other key is that these toxicities resolve with treatment," she added. "You need to give treatment to turn them around."

Conversely, toxicities associated with targeted therapy are predictable and dose dependent. Patients may react adversely to a starting dose of targeted therapy but go on to a good quality of life and outcome once the "perfect dose for them" has been found, said Ms. Burns.

Another important distinction is that while immune-related toxicities require treatment to resolve, adverse events associated with targeted therapy typically resolve with a treatment break.

THE ART OF TRIAGE AND INTERVENTION

Symptom attribution is a critical step in properly managing potential side effects, said Ms. Burns, who noted that the triage team of nurses and advanced practitioners plays a major role by asking the patient questions that get to the root cause of the problem. One question that needs to be asked is, "Are there causes other than treatment for the side effect that the patient is experiencing?" It's also important to ask about the timing and duration of the toxicity as well as its appearance. Finally, asking specific rather than general questions (e.g., "Is it shortness of breath or is it fatigue?") can help find attribution.

According to Ms. Burns, however, the first step of triage is actually educating patients about what to call for, when to call, and who to call. A skilled triage nurse or advanced practitioner who asks clear, objective questions will then help determine the intensity and grade of the symptom patients are calling about.

Ms. Burns provided some recommendations to advanced practitioners for ensuring patient safety, including always providing written ma-

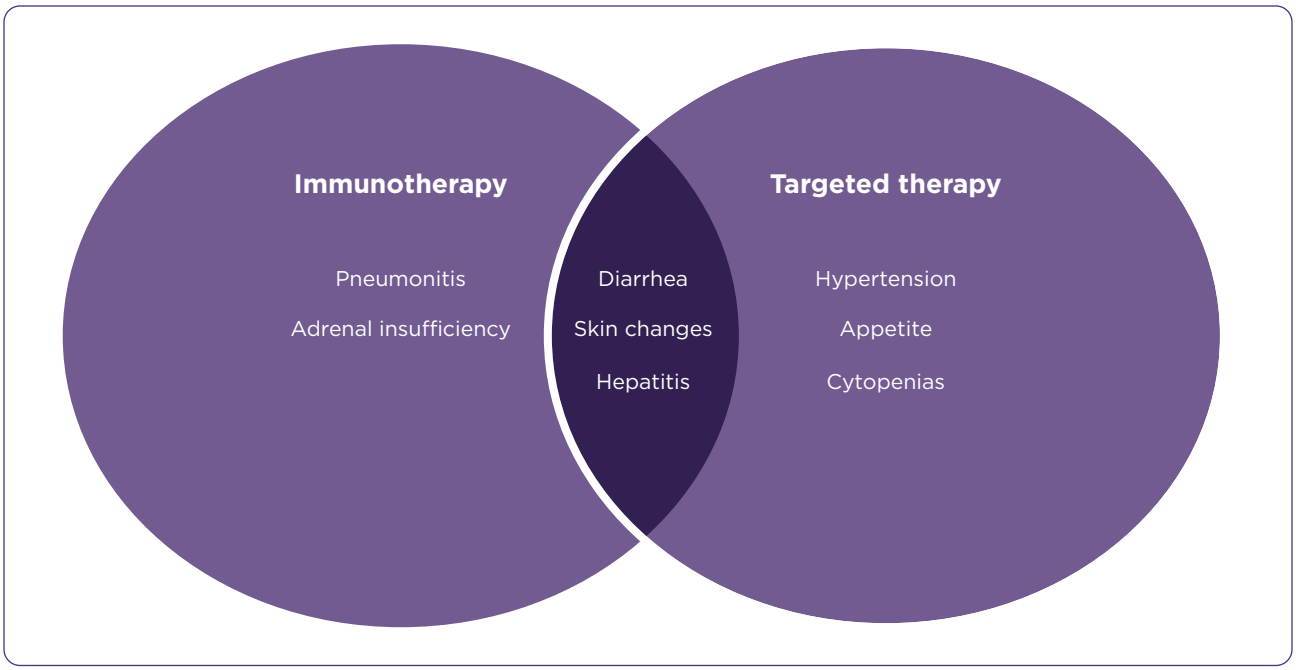

Figure 1. Common immunotherapy and targeted therapy toxicities.

terials, recommending websites or materials for patients to research drugs on their own, providing identification cards that list the names of the drugs patients are taking, overcoming language or communication barriers, using single rather than multiple pharmacies, and documenting dose adjustments clearly.

It's also important to ask patients how they have managed the symptom. While some patients are "afraid to take that into their own hands," said Ms. Burns, others try to manage rashes with skin products, for example, or change their diet with the onset of diarrhea.

One clinical pearl for targeted therapy is to simply hold treatment, although this can require managing patients' expectations.

TRACKING AND TREATING COMBINATION THERAPY

When there's a questionable attribution with combination regimens such as axitinib plus immunotherapy, toxicity management may require holding both drugs. If there's a quick resolution, it can be attributed to the targeted therapy. (Axitinib has a 6-hour half-life.)

If the toxicity is high grade, the agent should be permanently discontinued or held and restarted at a reduced dose. Immunotherapy would be continued, but if the toxicity is progressive after holding both agents, said Ms. Burns, the provider should initiate immunotherapy toxicity management protocol with workup and steroids.

"You should consider reexposure to immunotherapy with caution," she added. "If the toxicity is directly linked to an immuno-oncology drug, you could resume the targeted therapy once the steroids are tapered to less than 20 milligrams per day."

Ms. Burns provided some recommendations when working with combination therapy (Table 1).

Table 1. Tracking and Treating Combination Therapy

- Full assessment/grading/history
- Clear attribution to one drug or the other, or both
- Fully document any dose modification and why
- Teach the patient/family what to change verbally and in writing
- Follow up with a telehealth/in-person safety check

RESOURCES FOR MANAGING COMBINATIONS

Because not all providers practice in large cancer centers or institutions with multiple oncology experts, making the best choices for patients sometimes requires utilization of external resources. With respect to treatment, said Ms. Burns, the National Comprehensive Cancer Network (NCCN) Guidelines for the Management of Immunotherapy-Related Toxicities, a collaborative effort between NCCN and the American Society of Clinical Oncology (ASCO), is a useful reference when working combination treatment protocols (nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf).

"These Guidelines are great," she continued. "I'm always surprising myself by how often I look to those in clinic."

For those new to oncology, Ms. Burns also underscored the importance of networking.

"This is really the best part of oncology," she said. "My experience has always been that people love to share their knowledge and their expertise."

Finally, with respect to patient education, Ms. Burns recommended NCCN, chemocare.com, the Oncology Nursing Society, and ASCO websites as useful resources. ●

Disclosure

Ms. Burns has served on speakers bureaus for Amgen, Astellas, Exelixis, Merck, and Pfizer.