

KEY PRESENTATIONS FROM THE

Kidney Cancer Research Summit

ONCOLOGY reviews key presentations from the 2024 Kidney Cancer Research Summit. Highlights from the conference include advances in survival and the use of artificial intelligence to predict treatment outcomes. CN

Nivolumab Combo May Show Long-Term Benefits in Advanced RCC

Combining nivolumab (Opdivo) with ipilimumab (Yervoy) may potentially improve long-term outcomes in patients with advanced renal cell carcinoma (RCC) regardless of their International Metastatic RCC Database Consortium risk, according to findings from the phase 3 CheckMate 214 trial (NCT02231749).

Across the intent-to-treat population, the median overall survival (OS) was 52.7 months (95% CI, 45.8-64.5) in patients who received nivolumab/ipilimumab (n=550) compared with 37.8 months (95% CI, 31.9-43.8) in those who received sunitinib (Sutent; n=546; HR, 0.72; 95% CI, 0.62-0.83). Additionally, the median progression-free survival (PFS) was 12.4 months (95% CI, 9.9-16.8) vs 12.3 months (95% CI, 9.8-15.2) in each respective arm (HR, 0.88; 95% CI, 0.75-1.03).

Data highlighted an objective response rate (ORR) of 39% (95% CI, 35%-44%) with the nivolumab combination compared with 33% (95% CI, 29%-37%) with sunitinib. In each respective arm, 12% vs 3% of patients had complete responses (CRs) and 27% vs 29% had partial responses. Additionally, the median duration of response

(DOR) was 76.2 months (95% CI, 59.1-not evaluable [NE]) vs 25.1 months (95% CI, 19.8-33.2) in each respective arm (HR, 0.52; 95% CI, 0.38-0.72).

Among patients with favorable-risk disease, the median OS was 77.9 months (95% CI, 64.6-91.6) in those who received nivolumab/ipilimumab (n=125) vs 66.7 months (95% CI, 56.0-79.9) in those who received sunitinib (n=124; HR, 0.82; 95% CI, 0.60-1.13). The OS rates in each arm were 85.1% vs 88.4% at 24 months, 52.3% vs 46.4% at 72 months, and 42.8% vs 34.4% at 90 months, respectively.

Treatment yielded a median PFS of 12.4 months (95% CI, 10.3-18.0) and 28.9 months (95% CI, 23.2-42.8) in the nivolumab/ipilimumab and sunitinib arms, respectively (HR, 1.76; 95% CI, 1.25-2.48). Additionally, the PFS rates were 36.5% vs 58.5% at 24 months, 17.0% vs 17.0% at 72 months, and 12.7% vs 17.0% at 90 months in each respective arm.

The ORR across the favorable-risk population was 30% (95% CI, 22%-38%) with the nivolumab combination vs 52% (95% CI, 43%-61%) with sunitinib, and the CR rates were 13% vs 6% in each arm. Data showed a median DOR of 61.5 months (95% CI, 27.8-NE) vs 33.2 months (95% CI, 24.8-51.4) in each respective arm (HR, 0.70; 95% CI, 0.36-1.34). Additionally, 68% vs 66%, 37% vs 14%, and 37% vs



Abemaciclib May Show Synergistic Effect in Trials of Kidney Cancer Combination

Bradley A. McGregor, MD, discusses results from a phase 1b study (NCT04627064) assessing the efficacy of abemaciclib monotherapy in heavily treated patients with metastatic clear cell renal carcinoma.

To watch the full video, visit cancernetwork.com/KCRS24_McGregor

14% of patients in each arm had ongoing responses at 24 months, 72 months, and 90 months, respectively.

+ For full article and references visit cancernetwork.com/KCRS24_CheckMate214

Multimodal AI Approach May Predict Outcomes in Renal Cell Carcinoma

A multimodal artificial intelligence (AI) approach may help identify important elements for predicting outcomes in renal cell carcinoma (RCC). Specifically, investigators found that segmentation and partial volumetric analysis showed an improved chance of predicting postoperative kidney function. The presentation also highlighted that if this function could be quantified, personalization of RCC treatment might occur.

Investigators had 2 aims for researching this multimodal AI approach. The first was to develop an accurate and noninvasive AI tool to evaluate patient information, laboratory tests, and characteristics. These capabilities may allow investigators to differentiate between benign or indolent kidney masses and identify potentially aggressive tumors in the preoperative setting. The second aim was to establish an AI tool using preexisting data to estimate postoperative kidney function through nephron-sparing surgery or total nephrectomy.

Initially, the goal was to evaluate approximately 1000 to 1500 patients. However, with additional technologies such as pathology and the radiology pipeline, investigators plan to evaluate approximately 3000 patients. An additional 300 to 400 patients are being evaluated in a subset population for gene expression.

Investigators also recently submitted data regarding the age of patients. The hypothesis first focused on what it meant if the AI model incorrectly diagnosed a patient's age based on their CT scans. Results found that if the AI model thought the patient was younger than they were, they would be discharged earlier from the hospital than those who were predicted to be older than their actual age.

This was also observed in survival. If the AI tool predicted an age that did not correlate with the patient's actual age, it was predictive of better or worse outcomes. Investigators believe there are additional data to be extrapolated from these results because there hasn't been a way to truly analyze these outcomes before the development of this AI tool.



For full article and references visit cancernetwork.com/KCRS24_CheckMate214

Real-World Data Showcase Survival Outcomes After Immunotherapy/TKI Regimens in RCC

Patients with metastatic renal cell carcinoma (RCC) preferred tyrosine kinase inhibitors (TKIs) with or without immunotherapy-based treatments, according to results of a poster presented at the 2024 Kidney Cancer Research Summit. Investigators also highlighted that there was no difference in overall survival (OS) between the different immunotherapy- and TKI-based treatment regimens.

In the first-line setting, the most common postimmunotherapy treatments were axitinib (Inlyta) plus pembrolizumab (Keytruda; n=212), ipilimumab (Yervoy) plus nivolumab (Opdivo; n=156), immunotherapy monotherapy (n=34), cabozantinib (Cabometyx) plus nivolumab (n=19), and lenvatinib (Lenvima) plus pembrolizumab (n=12).

In the second line, the most common postimmunotherapy treatments were cabozantinib (n=197), cabozantinib plus nivolumab (n=53), other second-line options (n=46), axitinib or pazopanib (Votrient) or sunitinib (Sutent; n=42), ipilimumab plus nivolumab (n=40), axitinib plus pembrolizumab (n=24), everolimus



Ubatamab and Anti-PD-1 ICI May Bolster Immune Response in Kidney Cancer

Ubatamab in combination with an anti-PD-1 immune checkpoint inhibitor may enhance the immune response in patients with MUC16-expressing SMARCB1-deficient renal medullary carcinoma and epithelioid sarcoma, according to Pavlos Msaouel, MD, PhD.

To watch the full video, visit cancernetwork.com/KCRS24_Msaouel

(Afinitor) plus lenvatinib (n=15), and lenvatinib plus pembrolizumab (n=12).

In the third-line setting, 56 patients died, and 88 had ongoing treatment. Additional therapies included other third-line options (n=133), axitinib plus pazopanib and sunitinib (n=38), cabozantinib (n=38), ipilimumab plus nivolumab (n=10), everolimus (n=10), lenvatinib plus pembrolizumab (n=6), and nivolumab alone (n=4).



For full article and references visit cancernetwork.com/KCRS24_RCC

Manageable AEs Noted in Belzutifan for Advanced RCC

Safety remained manageable when belzutifan (Welireg) was used for patients with previously treated advanced clear cell renal cell carcinoma (RCC).

Results showed that of the 576 patients included in the analysis, 99.3% had at least 1 all-cause adverse effect (AE), and 61.6% experienced at least 1 AE that was grade 3 to 5 in severity. Serious AEs occurred in 41.0% of patients. AEs led to dose modifications in exactly half of patients, and this included reductions, interruptions, or discontinuations. The treatment discontinuation rate due to AEs was 6.4%. Nineteen patients (3.3%) experienced an any-cause AE that led to death.

All-grade and grade 3 to 5 treatment-related AEs were reported in 91.3% and 37.7% of patients, respectively. One death, due to multiple organ dysfunction syndrome, was reported to be related to belzutifan therapy.

Because of its unique mechanism of action and a historically distinct AE profile, investigators sought to evaluate belzutifan's safety profile across 4 clinical trials: phase 1 LITESPARK-001 (NCT02974738), phase 3 LITESPARK-005 (NCT04195750), phase 2 LITESPARK-013 (NCT04489771), and the von Hippel-Lindau disease-associated RCC cohort in the phase 2 LITESPARK-004 study (NCT03401788). Patients eligible to be included in the study had received at least 1 dose of belzutifan at 120 mg orally once daily across the 4 studies.

Investigators analyzed the severity of AEs per the National Cancer Institute's Common Terminology Criteria for Adverse Events version 4.03 or 5.0.



For full article and references visit cancernetwork.com/KCRS24_LITESPARK



To view the full conference coverage scan the QR code

Determining Administration of BCMA, T-Cell Engagers in R/R Multiple Myeloma



Joseph Mikhael, MD, MEd, FRCPC, FACP



Muhamed Baljevic, MD



C. Ola Landgren, MD, PhD



Cesar Rodriguez Valdes, MD



Saad Z. Usmani, MD, MBA, FACP, FASCO



Natalie Callander, MD



Joshua Richter, MD

The assessment of updated clinical trial data, optimal dosing strategies, and integration of bispecific antibodies into current relapsed/refractory multiple myeloma treatment paradigms were the focus of conversation during a *Frontline Forum*. Experts in multiple myeloma gathered to discuss these points of interest and experiences they have had in the clinic.

The panel was led by **Joseph Mikhael, MD, MEd, FRCPC, FACP**, professor in the Division of Applied Cancer Research and Drug Discovery at the Translational Genomics Research Institute, an affiliate

of City of Hope, in Phoenix, Arizona. He is also the chief medical officer of the International Myeloma Foundation.

He was joined by **Muhamed Baljevic, MD**, associate professor of medicine in the Division of Hematology-Oncology, director of the Plasma Cell Disorders Research of Vanderbilt-Ingram Cancer Center (VICC), director of the Vanderbilt Amyloidosis Multidisciplinary Program, and cochair of the VICC Protocol Review and Monitoring Program in Nashville, Tennessee; **C. Ola Landgren, MD, PhD**, professor of medicine, chief of the Division of Myeloma, director of the Sylvester Myeloma Institute, coleader of Translational and Clinical Oncology Program, and Paul J. DiMare Endowed Chair in Immunotherapy at the University of Miami Miller School of Medicine in Florida; **Cesar Rodriguez Valdes, MD**, associate professor of medicine at the Icahn School of Medicine at Mount Sinai, and clinical director of Multiple Myeloma at Mount Sinai Hospital in New York, New York; **Saad Z. Usmani, MD, MBA, FACP, FASCO**, chief of the Myeloma Service at Memorial Sloan Kettering (MSK) Cancer Center in New York, New York; **Natalie Callander, MD**, professor in the Division of Hematology, Medical Oncology, and Palliative Care at the University of Wisconsin School of Medicine and Public Health in Madison; and **Joshua Richter, MD**, associate professor of medicine in the Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai, director of Multiple Myeloma at the Blavatnik Family-Chelsea Medical Center at Mount Sinai and editorial advisor board member for *ONCOLOGY*.

Discovering the Ideal Talquetamab Dose

The panelists started by going through the data of important trials in multiple myeloma (Table¹⁻³). Regarding the MonumenTAL-1 trial, Richter commented that although there was a high response rate, duration of response and progression-free survival were significantly less. He noted that additional work is needed on this trial because although the response was high, it was not durable.

“It’s showing that every other week [dosing] is much more beneficial overall. I don’t think it’s changing our practice. All of us are already using [talquetamab] every other week, where it just reaffirms the fact that we’re on the right path,” Rodriguez said.

Baljevic said he believes talquetamab would be the preferred therapy for patients who have not been able to maintain adequate absolute neutrophil and absolute lymphocyte counts. He has also observed a difference in intravenous immunoglobulin (IVIG) replacement between bispecific antibodies and GPRC5D treatments.

Landgren wondered how this treatment would work with monthly dosing or perhaps in combination with another drug. Additionally, the weekly dosing was showing increased toxicities, which he noted was not viable for patients.

Callender said she recently had a patient who did not respond well to the step-up dose portion with talquetamab. Because of this and other experiences, she believes they’ll use the treatment more spaced out than the label recommends.

Mikhael asked Callender to elaborate on her approach and what responses she’s observed.

“[I dose-reduce] after cycle 1 very quickly. The response rates are fast; at least, that’s been my experience. I don’t know that you’re getting more benefit by just slamming patients [with doses once a week]; you’re just going to see more toxicity. I’m sure everybody else at this table is doing this too. This became our

preferred bridge with a short talquetamab course, particularly if they’ve been through a lot of other [lines of therapy]. You get a lot of benefits and skip a lot of the toxicity,” she said.

Another hot topic was treatment administration in an inpatient or outpatient setting. Richter admits patients for the first initial dose or so. If cytokine release syndrome (CRS) occurs, tocilizumab (Actemra) is administered, and the patients can go home within 24 hours.

Rodriguez, who works with Richter, noted that tocilizumab is administered at the first fever. Patients are also discharged with dexamethasone so if more symptoms arise, clinicians can instruct them to begin that course of treatment before coming in for an evaluation.

At Landgren’s institution, tocilizumab prophylaxis is given prior to the first treatment with a bispecific antibody. He conducted a study on the use of this with teclistamab and found the rate of CRS decreased from 75% to between 12% and 15%. Prophylaxis was also implemented with talquetamab and elranatamab.⁴

With talquetamab, a major issue has been taste-related adverse effects (AEs). Richter and Rodriguez have tried giving patients mouthwashes, supportive care measures, and even Oreo cookies to help tamp down these taste AEs but they have not had much success. The one thing that does seem to work is using lemon juice to stimulate the tongue’s taste receptors that are sensitive to sour tastes.

Rodriguez has tried giving patients dexamethasone plus nystatin 3 times a day from the first step-up dose of talquetamab. He believes this helps prevent oral inflammation and dysgeusia. He also recommended referencing *Flavorama*, a book written by a chef and biochemist that delves into how to enhance flavors.

Callender said that she believes dose holds rather than reductions are leading to a reduction in these taste AEs.

Improved Responses With Real-World Teclistamab Use

The conversation then transitioned to the use of teclistamab in the MajesTEC-1 study. “I’ve observed that the infection rates in the real world have been better than in studies because the prophylaxis approaches have, at least in my institution, been more organized and intense than what studies have mandated over time,” Baljevic said.

In terms of prophylaxis, he gives 10 g of IVIG to all patients. The results of this were presented at the 2023 American Society of Hematology Annual Meeting.⁵ Of the study’s 30 participants, 60% received GPRC5D therapies. There was not an increase in infections with this dosing. For those who did not respond well, 20 g of IVIG was administered to initiate a response.

Callender said she typically gives teclistamab to older patients but cautioned that they are more susceptible to infections.

Usmani noted that teclistamab de-escalation typically occurs after the third cycle. He arrived at this conclusion based on the time to best response and the discontinuation of patients who had a sustained response before a biochemical relapse.

At MSK, there is an outpatient administration model that includes any patient living 1 commutable hour from any MSK facility. Upon the first fever after treatment, patients are given acetaminophen (Tylenol). At the second fever, they are given dexamethasone, told to come in for an evaluation, and given tocilizumab in the clinic. Patients can be monitored for up to 6 hours if they’re still febrile; if they’re fine, they can go home.

Richter equates the early use of tocilizumab with helping prevent later flare-ups of infections.

“If you’re concerned about high-grade CRS in the older patients who are coming in with higher disease burden, you have to be selective. If we’re already saying that one-size-fits-all is not right for myeloma, we also

TABLE. Top Trials in Multiple Myeloma¹⁻³

TRIAL NAME	DRUG	EFFICACY	SAFETY
Phase 1/2 MonumentAL-1 (NCT03399799)	Talquetamab-tgvs (Talvey) at 0.4 mg/kg every week or 0.8 mg/kg every 2 weeks	ORR: 74.1% vs 69.5% DOR: 9.5 months vs 17.5 months PFS: 7.5 months vs 11.2 months	CRS: 79.0% vs 94.7% Taste-related: 72.0% vs 71.4% Nonrash skin-related: 56.6% vs 73.4%
Phase 1/2 MajesTEC-1 trial (NCT03145181; NCT04557098)	Teclistamab-cqyv (Tecvayli)	Median DOR: 24.0 months 30-month DOR rate: 45.0% Median PFS: 11.4 months 30-month PFS rate: 30.1%	TEAEs of any grade vs grade 3/4: 100% vs 94.5% Infection: 78.8% vs 55.2% Neutropenia: 71.5% vs 65.5%
Phase 2 MagnetisMM-3 trial (NCT04649359)	Elranatamab-bcmm (Elrexfio)	ORR: 61% CR: 35.0% VGPR: 56.1%	TEAEs of any grade vs grade 3/4 Anemia: 48.8% vs 37.4% Neutropenia 48.8% vs 48.8% CRS: 57.7% vs 0.0%

CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; ORR, overall response rate; PFS, progression-free survival; TEAEs, treatment-emergent adverse effects; VGPR, very good partial response.

have to be a little bit careful about how we say, ‘Tocilizumab for all.’ Maybe [it would work for] the patients with CAR [chimeric antigen receptor] T-cell therapy, where the proposition of CRS is very different. You’re concerned about mostly grade 2, grade 3 going to grade 4. With bispecific antibodies, it’s a little different,” Usmani said.

Regarding outpatient administration, Rodriguez noted that it’s feasible in academic centers, but the community setting may not be ready for it. Landgren agreed and said that this is why his institution had not gone to outpatient administration so quickly. Until the University of Miami was ready with a dedicated myeloma service, they could not trust that patients presenting to the emergency department with a fever would be treated for CRS and not an infectious disease.

Of note, Mikhael said that he has helped to create a curriculum to teach hospital internists how to properly diagnose CRS or immune effector cell–associated neurotoxicity syndrome.

Finding a Space for Elranatamab Treatment

A majority of the panel said they had not yet worked with elranatamab. Landgren has been able to use all 3 treatments at his institution, but because of financial calculations, he would stick with either teclistamab or elranatamab, the B-cell maturation antigens (BCMAs).

Baljevic, who has experience with

elranatamab, has not seen a difference when using this treatment compared with teclistamab or talquetamab. He noted that the formulary team could not justify adding it, but there had been experience administering it in studies.

Usmani echoed Baljevic’s sentiment saying he has experience with both elranatamab and teclistamab and has not seen a difference in terms of efficacy. Both are on the formulary at MSK, so it’s the principal investigator’s choice on which to use for their patients.

He did note that he and his colleagues gravitate a bit more toward teclistamab. Sometimes insurance influences the use of one vs the other and whether it can be administered as inpatient or outpatient, he said.

“The only difference is with fixed-dose vs weight-based dosing. There we’ve seen some interesting safety issues with patients [receiving] elranatamab where we are seeing some funky neurologic adverse effects, which were originally reported, but then we haven’t heard a lot about,” Usmani said.

Panelist Perspectives on Combining Treatments

Mikhael asked how the panel felt about combining talquetamab plus daratumumab (Darzalex).⁶ He wanted to know the rationale behind it: Was it because they have the same manufacturer or was there a biological reason?

Richter said he is not a fan of this combination specifically because it’s a

BCMA plus CD38. He prefers 2 mg of low dose pomalidomide (Pomalyst) plus talquetamab. Rodriguez agreed, especially because of the different AEs experienced with the combination. Usmani has been researching immune profiling and combining immunomodulatory drugs (IMiDs) with novel checkpoints.

“There’s some synergy with bispecifics and IMiDs, again with an effect on T-cell [therapy], that just seems natural. Based on our experience, less is more for the IMiD with these combos because you do have to be careful with them,” Callender said. ■

References

- Rasche L, Schinke C, Touzeau C, et al. Long-term efficacy and safety results from the phase 1/2 MonumentAL-1 study of talquetamab, a GPRC5DxCD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma. Presented at 2024 European Hematology Association; June 13–16, 2024; Madrid, Spain. Abstract P915.
- Garfall AL, Nooka AJ, van de Donk NWCJ, et al. Long-term follow-up from the phase 1/2 MajesTEC-1 trial of teclistamab in patients with relapsed/refractory multiple myeloma. *J Clin Oncol*. 2024;42(suppl 16):7540. doi:10.1200/JCO.2024.42.16_suppl.7540
- Tomasson M, Iida S, Niesvizky R, et al. Long-term efficacy and safety of elranatamab monotherapy in the phase 2 Magnetismm-3 trial in relapsed or refractory multiple myeloma (RRMM). *Blood*. 2023;142(suppl 1):3385. doi:10.1182/blood-2023-182130
- Kowalski A, Lykon J, Diamond B, et al. Emerging strategies for the prevention of immune toxicities associated with T cell-engaging cancer therapies. *Blood Cancer Discov*. 2024;5(2):90-94. doi:10.1158/2643-3230.BCD-23-0228
- Mameri N, Dholaria B, Sengsayadeth D, et al. Flat dose intravenous immunoglobulin primary infection prophylaxis in multiple myeloma patients on bispecific antibody therapy: Vanderbilt experience. *Blood*. 2023;142(suppl 1):3778. doi:10.1182/blood-2023-190749
- Dholaria BR, Weisel K, Mateos MV, et al. Talquetamab (tal) + daratumumab (dara) in patients (pts) with relapsed/refractory multiple myeloma (RRMM): updated TRIMM-2 results. *J Clin Oncol*. 2023;41(suppl 16):8003. doi:10.1200/JCO.2023.41.16_suppl.8003