

KIDNEY CANCER NEWS

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High Body Mass Index Linked to Improved Survival in Metastatic Renal Carcinoma

High body mass index (BMI) is associated with improved overall survival (OS) and progression-free survival (PFS) in people with metastatic renal cell carcinoma (mRCC), according to an analysis of 2 large patient cohorts. The researchers also found that fatty acid synthase (*FASN*) gene expression was downregulated among obese patients, supporting the hypothesis that these patients have a less aggressive subtype of RCC than normal-weight patients.

For the analysis, which appeared online September 6 in the *Journal of Clinical Oncology*, Dr Laurence Albiges and colleagues examined data on 1975 patients from 19 centers from the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC). Patients received targeted therapy with agents such as vascular endothelial growth factor (VEGF) inhibitors and mammalian target of rapamycin (mTOR) inhibitors.

After a median follow-up of 21.1 months, OS was significantly higher in patients who were overweight or obese (BMI, ≥ 25) than in those who were normal-weight or underweight (BMI, < 25), at 25.6 months (95% CI, 23.2-28.6 months) vs 17.1 months (95% CI, 15.5-18.5 months). The hazard ratio was 0.84 (95% CI, 0.73-0.95) after adjusting for IMDC prognostic factors.

Immunohistochemistry testing in 146 patients from the IMDC group revealed that *FASN* positivity was more frequent in poor-risk patients (11 of 23; 48%) and intermediate-risk patients (20 of 59; 34%) than in favorable-risk patients (5 of 30; 17%).

The researchers also examined data from a validation cohort of 4657 patients enrolled in phase 2 and 3 trials of sunitinib (Sutent, Pfizer), temsirolimus (Torisel, Pfizer), and axitinib (Inlyta, Pfizer). This cohort also revealed improved OS with high BMI vs low BMI: 23.4 months (95% CI, 21.9-25.3 months) vs 14.5 months (95% CI, 13.8-15.9 months), respectively. The adjusted hazard ratio was 0.83 (95% CI, 0.74-0.93).

Finally, the researchers analyzed genomic data on 61 patients with mRCC from the TCGA (The Cancer Genome Atlas) data set. They found that patients who had high BMI had significantly less expression of *FASN* compared with those who had low BMI, and that patients who had low *FASN* expression had significantly better median OS (36.8 vs 15.0 months; $P=.002$).

The authors concluded that fatty acid metabolism may play an integral role in the prognosis of patients with mRCC, which “lays the groundwork for future therapeutic interventions that target the FASN pathway.”

Observational Study Supports Use of Cytoreductive Nephrectomy in mRCC

Although the National Comprehensive Cancer Network (NCCN) recommends that all patients with mRCC receive cytoreductive nephrectomy (CN), the number of patients receiving the procedure has declined over the past decade—perhaps in response to the introduction of targeted therapy. Now, an observational study supports the use of CN in patients with mRCC who receive targeted therapy.

The study, which appeared online June 20 in the *Journal of Clinical Oncology*, encompassed 15,390 patients in the National Cancer Data Base who had mRCC and received targeted therapy between 2006 and 2013. A total of 35% of the patients underwent CN.

Dr Nawar Hanna and colleagues found that the patients most likely to undergo CN were white, younger, privately insured, and treated at an academic medical center. They also had a lower tumor stage and were less likely to have lymph node metastases.

The median OS was significantly higher for patients who received CN (17.1 months; 95% CI, 16.3-18.0 months) than for those who did not receive CN (7.7 months; 95% CI, 7.4-7.9 months; $P<.001$). The 3-year survival rates also were higher for those who received CN (27%; 95% CI, 26.3%-29.1%) than for those who did not (9.8%; 95% CI, 9.1%-10.5%).

The importance of nephrectomy in the current era is being addressed by 2 prospective randomized trials: CARMENA (the Clinical Trial to Assess the Importance of Nephrectomy) and SURTIME (the European Organisation for Research and Treatment of Cancer’s Immediate Surgery or Surgery After Sunitinib Malate in Treating Patients with Metastatic Kidney Cancer). Until the results of these studies are reported, wrote Dr Ana Molina and colleagues in a commentary that appeared online August 15, “CN remains the recommendation for patients with mRCC with a good performance status.”

Everolimus/Bevacizumab Benefits Patients With Non–Clear Cell RCC With Papillary Features

Combination treatment with a VEGF inhibitor plus an mTOR inhibitor appears to benefit patients with metastatic non–clear cell RCC if their disease has papillary features, according to a phase 2 study. Previous studies of the combination produced disappointing results, but were conducted primarily in patients with metastatic clear cell RCC.

The current study, published online September 6 in the *Journal of Clinical Oncology* by Dr Martin Voss and colleagues, was a single-center trial of 35 treatment-naïve patients with non–clear cell RCC. A total of 5 patients had chromophobe RCC, 5 had papillary RCC, 2 had medullary RCC, and 23 had unclassified RCC. All participants received everolimus (Afinitor, Novartis) 10 mg once a day plus bevacizumab (Avastin, Genentech) 10 mg/kg intravenously every 2 weeks.

Among the 34 patients who were evaluable, median PFS was 11.0 months, OS was 18.5 months, and the response rate was 29%. Evidence of benefit was driven by patients who had unclassified RCC with papillary features; these patients had a better median PFS (12.9 vs 1.9 months), OS (28.2 vs 9.3 months), and response rate (43% vs 11%) compared with those who had unclassified RCC without papillary features. In addition, 5 of 14 patients whose tumors had papillary features had somatic mutations in *ARID1A*—and all 5 benefited from treatment.

In a related editorial published online September 6, Dr Sumanta Pal and colleagues wrote that the results of the current study pave the way for further studies using VEGF inhibition plus mTOR inhibition.

Active Surveillance Safe for Some Patients With mRCC

Active surveillance before systemic therapy is safe for a subset of patients with mRCC, according to a phase 2 trial. Although retrospective studies had suggested that active surveillance was safe in these patients, this was the first prospective trial to examine the approach.

The study, by Dr Brian Rini and colleagues, enrolled 52 patients with mRCC that was treatment-naïve and asymptomatic. Radiographic assessments were carried out at baseline, every 3 months in year 1, every 4 months in year 2, and every 6 months thereafter. Observation

continued until the physician and patient decided to initiate systemic therapy. Results were published online August 3 in *Lancet Oncology*.

The median time on surveillance was 14.9 months (95% CI, 10.6–25.0 months) among the 48 patients in the analysis after a median follow-up of 38.1 months. More sites of metastatic disease and more adverse prognostic factors were each associated with a shorter period of surveillance. A total of 22 (46%) patients died of their disease during the study.

Although systemic therapy is standard in patients with mRCC, it is not curative in these patients, causes toxicity, and is costly. The investigators concluded that “active surveillance might be the optimum approach to avoid the certain toxicity of systemic therapy without clearly compromising the benefit of therapy when initiated.”

PD-1–Related Pneumonitis More Common in NSCLC, RCC Than in Melanoma

Pneumonitis related to programmed death 1 (PD-1) inhibitors is more common in non–small cell lung cancer (NSCLC) and RCC than in melanoma, according to a recent meta-analysis. PD-1–related pneumonitis also is more common with PD-1 combination therapy than with monotherapy.

Dr Mizuki Nishino and colleagues identified 20 studies in which patients with NSCLC, RCC, or melanoma received nivolumab (Opdivo, Bristol-Myers Squibb) or pembrolizumab (Keytruda, Merck) alone or in combination with ipilimumab (Yervoy, Bristol-Myers Squibb) or peptide vaccine.

Based on a total of 4496 patients, the researchers found that the overall incidence of pneumonitis with PD-1 monotherapy was significantly higher in NSCLC (4.1%) and RCC (4.1%) than in melanoma (1.6%). The incidence of grade 3 or higher pneumonitis with PD-1 monotherapy also was higher in NSCLC (1.8%) than in melanoma (1.5%), but was not higher in RCC than in melanoma. In addition, the overall incidence of pneumonitis was significantly higher with combination therapy (6.6%) than with monotherapy (2.7%).

The authors hypothesized that patients with NSCLC might be more likely to develop pneumonitis because of their underlying lung health. The cause of the increased risk of pneumonitis among patients with RCC remains to be determined.