Findings

Sunitinib without Nephrectomy for Metastatic Renal Cell Carcinoma

For patients receiving targeted therapies for metastatic renal cell carcinoma, outcomes are similar with sunitinib alone versus nephrectomy followed by sunitinib, concludes a trial in *The New England Journal of Medicine*.

The phase 3 randomized Clinical Trial to Assess the Importance of Nephrectomy (CARMENA) included 450 patients with biopsy-confirmed metastatic renal cell carcinoma, enrolled at 79 centers in France and other European countries. All were suitable candidates for nephrectomy followed by sunitinib. Memorial Sloan Kettering Cancer Center risk category was intermediate risk in about 58% of patients and poor risk in 42%.

After risk stratification, patients were assigned in a 1:1 ratio to nephrectomy followed by sunitinib (standard treatment) or sunitinib alone. Sunitinib dose schedule was 50 mg daily in cycles of 28 days on and 14 days off every 6 weeks. The main study endpoint was overall survival.

At planned interim analysis, with a median follow-up of 50.9 months, 326 patients had died. There was no significant difference in overall survival—the stratified hazard ratio for death fell below the specified boundary for noninferiority. Median overall survival was longer with sunitinib alone versus nephrectomy followed by sunitinib: 25.4 versus 19.0 months in the intermediate-risk group and 13.3 versus 10.2 months in the poor-risk group.

Response rate and progression-free survival were similar with or without nephrectomy. There was evidence of clinical benefit in 47.9% of patients in the sunitinib-alone group versus 36.6% in the nephrectomy-sunitinib group. Adverse events were as expected; dose reduction occurred in about 30% of both groups.

Cytoreductive nephrectomy has long been the standard of care for metastatic renal cell carcinoma. In recent years, new targeted therapies have emerged, including the vascular endothelial growth factor receptor inhibitor sunitinib. Few previous studies have directly compared the benefits of nephrectomy versus targeted therapy.

This randomized trial finds sunitinib alone non-inferior to nephrectomy followed by sunitinib in patients with intermediate- or poor-risk metastatic renal cell carcinoma. The findings contrast with those of retrospective studies reporting a survival benefit of nephrectomy in patients receiving targeted therapies. Although nephrectomy may have a role in controlling symptoms in some patients...there is no "late size fits all" approach," the investigators conclude [Méjean A, et al. Sunitinib alone or after nephrectomy in metastatic renal cell carcinoma. *N Engl J Med* 2018; DOI: 10.1056/NEJM-Moa1803675].

New Model Predicts Time to ESRD in Pediatric CKD

A new "six-risk-stage model" provides useful prognostic information for estimating time to end stage renal disease (ESRD) in children with chronic kidney disease (CKD), reports a study in the *American Journal of Kidney Disease*.

The analysis included data on 1169 children and adolescents enrolled in North American and European multicenter study cohorts: the Chronic Kidney Disease in Children (CKID) study and the Effect of Strict Blood Pressure Control and ACE Inhibition on the Progression of CRF in Pediatric Patients (ESCAPE) trial. Patients were classified according to three variables: glomerular filtration rate (GFR), estimated using the CKD “beside” equation; proteinuria, measured as first-morning urine protein-creatinine ratio (UPCR); and glomerular versus nonglomerular CKD diagnosis.

The investigators used these characteristics to define unique categories of CKD progression risk, along with estimated timelines to progression. The study definition of CKD progression was a composite of a 50% reduction in baseline GFR, decrease in eGFR to less than 15 mL/min/1.73 m², and/or dialysis or transplantation.

The patients were 707 males and 462 females, median age 12 years. All had a baseline eGFR of greater than 15 mL/min/1.73 m², with a median value of 47 mL/min/1.73 m². Initial UPCR was greater than 2 mg/mg in 13% of patients; 755 had nonglomerular diagnoses.

Median time to CKD progression exceeded 10 years for children with an eGFR of 45 or 90 mL/min/1.73 m² and UPCR less than 0.5 mg/mg. In contrast, for those with an eGFR of 15 to 90 mL/min/1.73 m² with a UPCR of greater than 2 mg/mg, median time to progression was 0.8 years. Within the various risk stages, time to progression was 43% shorter for children with nonglomerular CKD. Pediatric CKD is an uncommon problem associated with reduced life expectancy and high costs. The Kidney Disease: Improving Global Outcomes (KDIGO) classification system was developed to predict the risk of adverse outcomes and guide management strategies for adults with CKD. The researchers sought to develop a modified KDIGO classification system for pediatric CKD.

"This classification system can be used as an adjunct to clinical judgment in planning for timing of transplantation evaluation or dialysis access placement,” the researchers write. The online version of their article includes a printable page summarizing the six risk groups and their associated times to CKD progression events [Furch SL, et al. Estimating time to ESRD in children with CKD. *Am J Kidney Dis* 2018; 71:783–792].

“Emergency-Only Dialysis” Policy Puts Burdens on Clinicians

Following emergency-only hemodialysis (EOHD) policies for undocumented immigrants causes moral distress and may contribute to burnout among healthcare professionals at safety-net hospitals, reports a qualitative study in *Journal of Internal Medicine*.

The researchers interviewed 50 physicians, nurses, and other clinicians at safety-net hospitals/systems in two cities (Denver and Houston) that provided a high volume of EOHD for undocumented patients. Thematic analysis was performed to describe the experiences and perspectives of clinicians providing this type of care.

Four major themes were identified. Emergently only dialysis policies contributed to drivers of professional burnout, with healthcare professionals experiencing emotional exhaustion related to patients’ “needless suffering” and high mortality. Clinicians felt they had to “emotionally dissociate” themselves due to a policy that was not under their control. They also reported moral distress related to EOHD policies. All participants felt that it was unethical to make care decisions based on nonmedical factors, and felt justified in “bending the rules.”

Clinicians were frustrated over the “confusing and perverse” financial incentives associated with EOHD, which they viewed as an inefficient and unsustainable use of hospital and system resources. Despite their distress and frustrations, the healthcare professionals felt inspired by their patients’ resilience, kindness, and gratitude. Clinicians felt that working with these patients provided them an opportunity to act according to their best instincts and “motivated them to advocacy.”

In many states, undocumented immigrants with ESRD do not receive dialysis until they develop life-threatening renal failure. This EOHD policy leads to high mortality and distress for patients, but little is known about its impact on clinicians.

“The burden on clinicians of providing EOHD should inform policy discussions and systemic approaches to support provision of an adequate standard of care to all patients with ESRD,” the investigators said. [Cervantes L, et al. Clinicians’ perspectives on providing emergency-only hemodialysis to undocumented immigrants: a qualitative study. *Am Intern Med* 2018; DOI: 10.7326/M18-0400].