

New Campaign Seeks to Reduce Mortality for First-Year Dialysis Patients

By Brande Victorian

A coalition of patient advocates, nephrology professionals, and manufacturers has launched a new campaign pledging to slash mortality rates among first-year dialysis patients 20% by the year 2012.

Led by Kidney Care Partners (KCP), the quality improvement initiative, called PEAK (Performance Excellence and Accountability in Kidney Care), is bringing



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together experts in the nephrology community to improve care for this segment of the kidney disease population. Research partners at Brown University and Quality Partners of Rhode Island are also providing support.

“The campaign is just a means to recognize what the entire renal community feels,” said Edward Jones, MD, President of the Renal Physicians Association (RPA), which is a KCP member organization, in a phone interview.

“We need to approach the delivery of care differently, particularly with dialysis patients, who have a very high first-year mortality rate despite the good that we’ve been doing over the years. . . .

“The industry has been working hard, and the RPA has been actively involved with quality performance for a number of years. Approaches to things like this dealing with mortality are a real challenge. We are taking on probably one of the biggest challenges there is in delivering quality care to patients with end-stage renal disease.”

‘Aggressive Goal’

Reducing mortality by 20% in the next three years would save “thousands and thousands” of lives, said KCP Chair Kent Thiry in a phone interview.

“We wanted to have an aggressive goal because that would force people to really consider doing things differently. If you

had a more conservative goal that you were more comfortable about achieving, you’d be too comfortable sticking more or less with what you do now,” said Mr. Thiry, who is Chairman and CEO of DaVita, Inc., another KCP member.

“Once you have that aggressive goal that is going to provoke aggressive thinking, you need to make sure there is time to do the thinking, to experiment—to find out what works—and then to spread the good word about what works and get that implemented.

“That takes time, and so putting all of that together—bold goal, aggressive thinking, and time to experiment and share—meant that the end of 2012 was the amount of time it was going to take to give us a chance.”

The focus of the campaign is to supply health care providers with tools to help first-year dialysis patients better transition into therapy and to improve their overall health and survival, with the additional intended effects of a reduction in hospitalizations and Medicare savings.

While the specifics are still being determined, there are several areas of opportunity, Mr. Thiry noted.

“One is increasing the amount of patient education in those early months where we’ve found that patient retention is more spotty, the second is increased involvement with families in education, the third is more frequent care plans, and the fourth is tools that are



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more focused on some of the issues that incident patients face, particularly in the areas of albumin, access, adequacy, and anemia. Those are . . . specific areas where we’ve found that by doing more or doing things differently we can make a big difference.”

Drawing on Organizational Expertise

All 33 KCP member organizations have
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Education

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Stony Brook University School of Medicine is heading in that direction as well, said Richard N. Fine, MD, who is the Dean there and a pediatric nephrologist.

“We are moving in many areas toward competency-based education; this is not sparkling rocket news.” Dr. Fine said he agrees with the report’s recommendations, noting that the Liaison Committee on Medical Education (LCME) medical education accreditation standards are competency based.

It is not enough for medical students to simply be able to identify a particular condition, he added.

In terms of the nephrotic syndrome, for example, medical students must have the analytical ability to understand the pathophysiological mechanisms that underlie the condition, Dr. Fine said. “Once you know that, you can target the treatment.”

The report’s emphasis on lifelong learning is also crucial, Dr. Fine added. “Information in the biomedical sciences does not end after medical school. . . . It’s a continuum throughout life.”

The vastness of medical information and the swiftness with which it changes is true of all medical fields, including nephrology.

For example, said Dr. Fine, when new drugs for recipients of a kidney transplant come onto the market, a nephrologist needs the skills to evaluate the manufacturer’s claims for these new medications and decide if they are right for his or her patients.

In addition to addressing competencies that engage students’ inquisitiveness, the report highlights the importance of medical professionalism, which has been integrated into the Stony Brook curriculum, Dr. Fine said.

“In the past it was relatively easy to pick out medical students at both ends of the spectrum—those who plagiarized or were disruptive versus those who were ex-



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tremely compassionate and empathetic with patients—but now that it is integrated into the curriculum, professionalism can be better identified in all students.”

Boost Number of Physician-Scientists

Rethinking medical school curricula makes sense given the relative decline in the number of physicians who are doing research and adding new knowledge to the profession, said nephrologist Robert W. Schrier, MD, Professor of Medicine and former Chair of the Department of Medicine at the University of Colorado School of Medicine, who had not yet seen the new report.

“We need to excite these young medical students and doctors to pursue basic and clinical research. This is a time where the tools available for research and understanding disease and intervening in disease have never been more exciting.

“I think what we need to do is make sure we take the cellular and molecular biology and indicate the implications for physiology and pathophysiology. . . . That’s the future of medicine in nephrology.” •

Peak

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signed on to be part of PEAK, and the coalition is also inviting non-members to join the campaign.

“[P]art of our excitement and the genesis of this idea is that a number of organizations, including DaVita, have done programs focused on incident patients,” Mr. Thiry said.

Such programs like IMPACT (Incident Management of Patients, Actions Centered on Treatment) from DaVita and RightStart from Fresenius Medical Care—initiatives centered on patient education and management of key clinical outcomes during the first 90 days of dialysis—have resulted in reduced mortality among the patient populations studied and will likely be incorporated into the PEAK campaign on a larger scale.

“How we’re going to deal with PEAK will largely grow from the RightStart work we did,” said Kathleen T. Smith, RN, BS, CNN, Vice President for Governmental Affairs with Fresenius Medical Care North America, in a phone interview.

The American Kidney Fund (AKF), an organization that provides financial assistance to approximately 75,000 patients with kidney disease, plans to extend its role in helping patients with end-stage renal disease (ESRD) pay health insurance premiums and maintain access to medical care, as well as spread the word about PEAK.



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“We will link to the PEAK Web site, and we will include information on PEAK in our many publications,” said AKF President and CEO LaVarne A. Burton in a phone interview.

“We want to help get out the information, make sure that people are aware of PEAK, and make them aware of where they can go to access the learning center and get information that will help them serve patients even better than they already are, and to help patients obtain information as well.”

Sharing Best Practices

Kidney Care Partners is currently working with the Centers for Medicare and Medicaid Services (CMS) to develop a database for accurately measuring indicators of improvement so that the campaign’s progress can be properly assessed.

Interim reporting will be part of the campaign, but the schedule won’t be finalized until CMS determines how frequently it can provide data. The coalition

is also putting together expert panels to tackle each area of improvement.

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Belatacept

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nephrotoxicity and increased cardiovascular and metabolic risks associated with calcineurin inhibitors (CNIs), noted Flavio Vincenti, MD, Professor of Clinical Medicine in the Division of Nephrology at the University of California, San Francisco (UCSF), as he presented the primary results from the Belatacept Evaluation of Nephroprotection and Efficacy as First-Line Immunosuppression (BENEFIT) Phase III trial (*Abstract #4*).



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"It's clear that we need novel immunosuppression to improve outcomes," Dr. Vincenti said. "Belatacept immunosuppression regimens better preserve kidney function and structure and improve the cardiovascular risk profile compared with cyclosporine."

However, patients given belatacept had higher rates of acute rejection than those given cyclosporine: 22% in the more-intensive belatacept arm (MI), 17% in the less-intensive belatacept arm (LI), and 7% in the cyclosporine arm. The less-intensive regimen was non-inferior to cyclosporine for this endpoint, but the more-intensive regimen did not meet the non-inferiority margin.

Peak

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demonstrations that have been conducted, it's been shown that we can make significant increases in survival rates, and that has been done when you focus on this initial entry into dialysis," Ms. Burton said.

"We want to take those best practices that we've learned through demonstrations and other practices and share them throughout the community so that all patients are able to benefit from them." •

"People get focused on acute rejection, but over the past 10 years we've dropped acute rejection from 40% to below 15%," Dr. Vincenti said in an interview after the presentation. "We have not improved long-term graft survival by one iota."

"I'm not saying I think rejection is not important. All I'm saying is that lowering rejection by itself has not been sufficient. I think the renal function trumps rejection."

During the presentation, Dr. Vincenti noted, "Even patients who had rejection with belatacept MI and LI had much better renal function than those patients on cyclosporine who did not get rejection."

John Roberts, MD, who co-moderated the session during which the results were presented, said he would have liked to have seen a lower rejection rate with belatacept.

"We're going to need to understand how to take advantage of belatacept's lack of nephrotoxicity but decrease the rate of rejection," said Dr. Roberts, Chief of the

Transplant Service at UCSF, in an interview at the meeting.

In these higher rejection rates may lie a parallel between belatacept and mammalian target of rapamycin (mTOR) inhibitors, said Matthew Weir, MD, Professor of Medicine and Director of the Division of Nephrology at the University of Maryland School of Medicine, in an interview at the meeting.

"There may be the same problem there as we saw with all the early mTOR inhibitor studies where belatacept may be an approach you start to use after three to four months, after you induce with cyclosporine and tacrolimus, and then you convert them over."

"With mTOR there was more rejection, but what we see now is if anything there's less later acute rejection. The other question, too, is you've always got to know drug levels, drug levels, drug levels."

Three Primary Endpoints

In the study, 666 adult kidney trans-

plant recipients were randomized to receive more-intensive belatacept (219 patients), less-intensive belatacept (226 patients), or cyclosporine (221 patients). All patients received basiliximab induction, mycophenolate mofetil (MMF), and corticosteroids. (*To read about outcomes with belatacept in recipients of an extended-criteria donor kidney, please see the box*).

The anticipated cold ischemia time for all donor organs was less than 24 hours; 58% of patients received a kidney from a living donor, and 42% from a deceased donor.

The co-primary endpoints were: 1) a composite of patient/graft survival, 2) composite renal function (measured glomerular filtration rate [mGFR] less than 60 mL/min/1.73 m² at Month 12 or a decrease in mGFR of 10 mL/min/1.73 m² or more between Months 3 and 12), and 3) incidence of acute rejection. The 12-month results of this three-year study were presented at the meeting.

About 20% of patients in each arm

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In ECD Kidney Recipients, Renal Function Superior with Belatacept

In recipients of a kidney transplant from an extended-criteria donor (ECD), renal function was better—and patient/graft survival and acute rejection similar—with an immunosuppression regimen based on belatacept versus one based on cyclosporine. This was the conclusion of research presented here at the American Transplant Congress, the joint annual meeting of the American Society of Transplant Surgeons (ASTS) and the American Society of Transplantation (AST).

Belatacept is a first-in-class costimulation blocker designed to avoid the nephrotoxicity and increased cardiovascular and metabolic risks associated with calcineurin inhibitors.

Included in the three-year Phase III trial, called Belatacept Evaluation of Nephroprotection and Efficacy as First-Line Immunosuppression—Extended Criteria Donors (BENEFIT-EXT), were 543 adult recipients of an extended-criteria donor kidney randomized to receive a more-intensive regimen of belatacept (MI; n=184), a less-intensive regimen of belatacept (LI; n=175), or cyclosporine (n=184) (*Abstract #27*). All patients received basiliximab induction, mycophenolate mofetil, and corticosteroids.

The two coprimary endpoints were 1) a composite of patient/graft survival at 12 months and 2) composite renal function (measured glomerular filtration rate [mGFR] greater than 60 mL/min/1.73 m² at Month 12 or a decrease in mGFR of 10 mL/min/1.73 m² or more from

Month 3 to Month 12. Incidence of acute rejection (AR) was one of the secondary endpoints.

As had been seen in the BENEFIT study, which included adult recipients of a living- or deceased-donor kidney (see *article on page 1 of this issue of Nephrology Times*), patient and graft survival with a functioning kidney were similar across the treatment groups—86% for MI, 88% for LI, and 85% for cyclosporine.

The incidence of acute rejection was comparable across all three arms of the study in ECD recipients.

Renal function was significantly better in the more-intensive belatacept arm than in the cyclosporine arm: In the MI group, 71% of patients reached the composite renal endpoint, and the measured GFR was 52 mL/min at Month 12, while in the cyclosporine group 85% of patients reached the composite renal endpoint, and the mGFR was 45 mL/min at Month 12. In the LI group, 76% of patients reached the composite renal endpoint, and the mGFR was 50 mL/min at Month 12—values that did not significantly differ from those found in the cyclosporine arm.

Unlike BENEFIT, the incidence of

acute rejection was comparable across all three arms of BENEFIT-EXT, between 14% and 18%.

"The recipients of these extended-criteria kidneys are quite old patients with a low immunologic risk," said J. M. Campistol, MD, PhD, who presented an abstract focusing on the preservation of renal function and structure with belatacept in ECD kidney recipients, when asked about the difference between the two studies in an interview. Dr. Campistol is from the Department of Nephrology and Urology at Hospital Clinic of the University of Barcelona.

Cardiovascular and metabolic outcomes again were superior with belatacept, and overall rates of infection and malignancy remained comparable.

The incidence of posttransplant lymphoproliferative disorder (PTLD) was higher in the belatacept groups: During the first 12 months, there was one case or PTLT in the MI group (0.5%), two in the LI group (0.9%), and none in the cyclosporine group, and, after 12 months, there was one case each in the MI and LI groups. Most cases of PTLT occurred in recipients with known risk factors.

"The only concern I think is about PTLT in these high-risk patients—we probably need to do prophylaxis," Dr. Campistol said.

In terms of next steps, longer term follow-up is needed, he added.

"The data we presented today is from one-year follow-up, so it is a short time. The good thing will be to check three years and five years."