

Drug May Prolong Organ Life in Non-Compliant Kidney Transplant Patients

UC San Diego Researchers Present Findings at American Transplant Congress

May 30, 2008

Kim Edwards

New research from the University of California, San Diego Department of Medicine, Division of Nephrology, shows that the anti-rejection drug sirolimus (brand name Rapamune) may help prolong the clinical benefit of transplanted kidneys and delay rejection, especially in patients who do not regularly take their prescribed medications (are "non-compliant"). While the transplant field has been highly successful at reducing rejection and graft loss in the first year, post-transplant, reducing risk for graft rejection in the long-term has proved more difficult.

The findings are being presented at the 2008 American Transplant Congress (ATC), in Toronto on Saturday, May 31, 2008, by Cheri Ye, M.D., who was mentored by Robert Steiner, M.D., professor of medicine, and Director of Transplant Nephrology.

"No one is perfect at taking medications," explained Steiner. "But missing doses of immunosuppression, or not taking full doses each day, will bring about gradual rejection of kidney transplants that is almost impossible to detect in its early stages. Long acting drugs like sirolimus may help with this problem."

A team of five UC San Diego investigators reported a careful assessment of immune function at "trough" levels (lowest daily levels) of the three most commonly used immunosuppressive drugs, using an assay (ImmuKnow®/Cylex) designed specifically to measure the degree of immunosuppression at any given time. Lower "mitogenic response" meant better immunosuppression and more protection from rejection. On average, the participants, 160 kidney transplant patients, were 6.4 years out from their transplant.

At these trough levels of drug in the blood stream, the assay demonstrated that sirolimus caused a significantly lower level of mitogenic response, and results appeared to be stable in individual patients over time.

"At least half of transplanted kidneys are lost through chronic graft rejection, usually within 10 years. When patients do not have those rejection problems, they can go for 20 to 30 years before kidney rejection or other serious problems. This is an especially important issue now because of our nationwide donor-organ shortage," said coauthor, David Perkins, M.D., Ph.D., professor of medicine & surgery, and Director of Research for Transplantation.

"This study was not commercially funded," added Steiner. "We just wanted to confirm what we suspected from experience in our transplant clinic, where we focus on compliance in many ways to help our patients keep their kidneys functioning well. We showed that when the daily dose is wearing off and another dose is due to be taken, patients taking sirolimus could be more protected against rejection than other commonly used agents."

The assay used is the only commercially available of its kind, and potentially valuable, but researchers emphasized that experience and understanding of it is limited.

"Our ATC abstract is a report of clinical experience, but real progress is often made at the level of basic science. My laboratory is studying this intensively at a basic level in several ways, including looking at the genetics associated with various responses to the assay," said Perkins.

The researchers believe that this new study may help develop tools to monitor patients in the long-term, and also contribute to a protocol for using sirolimus in less compliant patients. Steiner pointed out that, "The best results will occur if we prevent rejection, because once rejection is established the threat to graft survival is much greater, no matter what we do."

Co-authors of the study, "*Sirolimus (SRL) Blunts Mitogen Response at Trough (C0) Levels More Than Cyclosporin (CSA) or Tacrolimus (TAC): A Safeguard for Our Many Long Term Noncompliant Kidney Transplant Patients (KTPs)*" include UC San Diego School of Medicine physicians Nitin Khosla M.D., and Rodolfo Batarse, M.D., assistant professor of medicine.

About ATC The ATC is the premier educational event in the field of basic and clinical transplantation, with the widest range of educational opportunities. Topics range from toll-like receptors and composite limb grafts to recent immuno-suppression trials and issues in the globalization of transplantation.

The American Society of Transplant Surgeons (ASTS) was founded in 1974 in an effort to unite surgeons involved in the fledgling field of transplantation. Since then, the Society has established a strong presence in transplantation research, education and training, and advocacy.

The American Society of Transplantation (AST) was founded in 1982 and is an organization of more than 2,600 transplant professionals dedicated to research, education, advocacy and patient care in transplantation. AST's goal is to offer a forum for the exchange of knowledge, scientific information and expertise in the field of transplantation.

About UCSD Center for Transplantation The UCSD Center for Transplantation at UCSD Medical Center performed San Diego County's first kidney transplant in 1968 and has since performed more than 2,000 kidney transplants on patients of all ages. In 1999, the kidney transplant program began using a new, less invasive technique for living kidney donation, using endoscopic instruments through very small incisions. In addition, UC San Diego Medical Center's clinical research programs are at the forefront of discovering new information on the biology of organ rejection, organ preservation and long-term medical management for transplant recipients.

Media Contact: Kim Edwards, 619-543-6163