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## **KIDNEY TRANSPLANT PATIENTS MAY BENEFIT FROM GOING OFF OF CERTAIN IMMUNOSUPPRESSIVE DRUGS**

*Withdrawal of Calcineurin Inhibitors Provides Long-term Health Benefits and Saves Money*

**Washington, DC (Tuesday, June 17, 2008)** — Withdrawing certain immunosuppressive drugs following kidney transplantation prolongs survival and saves money compared with keeping patients on these medications for life, according to a study appearing in the September 2008 issue of the *Journal of the American Society Nephrology* (JASN). In this study, a lifetime Markov model was created to compare the cost-effectiveness of a sirolimus-based calcineurin inhibitor (CNI) withdrawal regimen (sirolimus plus steroids) with other common CNI-containing regimens in adult *de novo* renal transplantation patients. The findings indicate that in the long-run, the risks of the medications potentially outweigh their benefits.

Immunosuppressive drugs such as calcineurin inhibitors are critical after kidney transplantation to prevent organ rejection, particularly during the first year. However, a trade-off exists, because calcineurin inhibitors are associated with serious adverse effects, including renal dysfunction, infections, cancer, diabetes mellitus and cardiovascular-related events. Therefore, regimens need to be optimized over time so that patients can benefit from the drugs' short-term benefits but not be harmed by their long-term risks.

Head-to-head analyses of the short-term benefits and long-term risks of calcineurin inhibitors are limited. To compare the two, Dr. Stephanie Earnshaw of RTI Health Solutions in Research Triangle Park, NC, and her colleagues examined data from published studies and from the United States transplant registry. The investigators developed a decision-analytic model to assess long-term donor kidney survival, short- and long-term patient outcomes, and costs.

Sirolimus, in combination with steroids, is currently the only immunosuppressive treatment regimen that is approved for use when calcineurin inhibitors are withdrawn. Therefore, Dr. Earnshaw's group compared treatments containing sirolimus plus steroids versus treatments that maintained the use of calcineurin inhibitors.

The researchers' decision-analytic model, using data published in the literature and reported by the US transplant registry, assumed that within the first 12 months following transplant surgery, sirolimus plus steroid therapy is associated with a greater risk of kidney allograft rejection than regimens that continue to use calcineurin inhibitors. Other commonly used regimens include a calcineurin inhibitor such as cyclosporine or tacrolimus, plus mycophenolate mofetil and steroids. In this particular study, it was assumed that in the absence of induction therapy a total of 21.8% of patients taking sirolimus plus steroids experienced acute rejection within one year of transplantation, compared with 19.0% of patients taking cyclosporine plus mycophenolate mofetil and steroids, and 17.1% of patients taking tacrolimus plus mycophenolate mofetil and steroids.

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However, it was revealed that overall, treatment with sirolimus plus steroids may be more efficacious and less costly than regimens that continued to use calcineurin inhibitors. Specifically, withdrawal of calcineurin inhibitors may prolong patients' lives and improve their kidney function.

It was estimated that the average number of grafts lost per patient over their remaining lifetime after initial kidney transplantation (patients can have more than one transplant) was 0.90 for patients taking sirolimus plus steroids, compared with 0.94 for patients in the cyclosporine group and 0.92 for patients in the tacrolimus group. Sirolimus plus steroids also may increase patient survival (11.43 years, compared with 11.37 years in the cyclosporine group and 11.13 years in the tacrolimus group.) Total lifetime costs per patient in the three groups were \$472,799; \$484,020; and \$505,420, respectively.

According to the authors, these findings indicate "calcineurin inhibitor withdrawal not only shows potential for long-term clinical benefits, but also is expected to be cost-saving over a patient's life compared with the most commonly prescribed calcineurin inhibitor-containing regimens." They note that withdrawal of CNIs is an important option because clinicians consider the lifetime of the patient to be more important than the year that follows transplantation. It is important to note that this analysis relied on certain assumptions (such as the incidence of acute rejection per treatment arm and measures of renal function) due to limited availability of data. As such, additional research will be necessary to support these results.

Funding for this analysis was provided by Wyeth Pharmaceuticals in Collegeville, PA.

The article, entitled "Cost-Utility of Calcineurin Inhibitor Withdrawal After de Novo Renal Transplantation," authored by Stephanie R. Earnshaw<sup>1</sup>, Christopher N. Graham<sup>1</sup>, William D. Irish<sup>1</sup>, Reiko Sato<sup>2</sup>, and Mark A. Schnitzler<sup>3</sup> (<sup>1</sup>RTI Health Solutions, <sup>2</sup>Wyeth Research, <sup>3</sup>St. Louis University) will be available online at <http://jasn.asnjournals.org/> beginning on Wednesday, June 18, 2008 and in the September 2008 print issue of JASN.

ASN is a not-for-profit organization of 11,000 physicians and scientists dedicated to the study of nephrology and committed to providing a forum for the promulgation of information regarding the latest research and clinical findings on kidney diseases. ASN publishes JASN, the *Clinical Journal of the American Society of Nephrology* (CJASN), and the *Nephrology Self-Assessment Program* (NephSAP). In January 2009, ASN will launch a newsmagazine.

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