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News Release

For Immediate Release

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NEW STUDIES OF IMMUNOSUPPRESSIVE REGIMENS LIMITING OR AVOIDING THE USE OF STEROIDS SHOW EXCELLENT GRAFT SURVIVAL IN TRANSPLANT RECIPIENTS ON A PROGRAF®-BASED (TACROLIMUS) REGIMEN

One Study of Early Steroid Withdrawal
Reduced Cholesterol Levels and Decreased Onset of Post Transplant Diabetes

SEATTLE, May 24, 2005 -- Early steroid withdrawal along with the use of tacrolimus (TAC or Prograf®) and mycophenolate mofetil (MMF) resulted in more than 98 percent patient survival and 100 percent death-censored kidney graft survival at one year, according to a new study presented today at the 6th American Transplant Congress (ATC). Results also revealed a reduction in total and low density lipoprotein (LDL), the main source of cholesterol buildup and blockage in the arteries. Additionally, in this study, fewer patients in the early steroid withdrawal group developed post-transplant diabetes mellitus (PTDM) requiring insulin, and fewer patients experienced weight gain, as compared to the chronic steroid therapy group. There was a significant increase in biopsy proven acute rejection and moderate to severe acute rejection in the early steroid withdrawal group, although the mean MMF dose was lower in this group.

A separate pediatric study found that a steroid-free immunosuppressive regimen in kidney transplant patients ranging in age from one to 20 years, with the use of TAC, MMF and Daclizumab (Zenapax®*) resulted in 100 percent graft survival after one year with fewer episodes of acute rejection and cytomegalovirus (CMV) disease compared to the steroid-based control group.

In yet a third study of cadaveric kidney recipients, TAC-based steroid-free therapy provided equivalent acute rejection and patient and graft survival at two years in both African-American and non African-American groups. In addition, the incidence of PTDM was low in both groups – 4 percent (AA) and 2 percent (non AA).

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"This study indicates that elimination of corticosteroid therapy within 7 days of transplantation, when compared to long-term low dose corticosteroid therapy, is associated with a small increase in the risk of acute rejection, but this effect is countered by improvements in cardiovascular risk," said E. Steven Woodle, MD, FACS, Professor of Surgery, University of Cincinnati Hospital and lead investigator of the corticosteroid cessation study. "These early results provide evidence of the advantages of steroid-sparing regimens that are being employed with increasing frequency in renal transplantation."

Early Corticosteroid Cessation Versus Chronic Corticosteroid Maintenance Therapy

The randomized, double blinded study compared corticosteroid withdrawal (CSWD) on post-transplant day (PTD) seven to chronic corticosteroid therapy (CCS) under tacrolimus (TAC) / mycophenolate mofetil (MMF) with antibody (ab) induction. Patients were required to meet the rigid inclusion and exclusion criteria to participate in the study. The primary endpoint of the study was treatment failure (death, graft loss, or moderate acute rejection). Investigators and patients will remain blinded for five years. The one-year follow-up of nearly 400 patients, 195 CCS and 191 CSWD respectively, found no differences occurring in the primary endpoint (96.9/93.7%), patient survival (98.5/99.5%), death-censored graft survival (100/99.5%), all infections (30.8%/28.8%), CMV disease (10.2/6.3%), fungal infections (6.1/3.1%), lymphoma (0.5/0.5%). A significant difference occurred in bx-proven acute rejection (AR) (6/12%, p=0.04) and moderate/severe AR (1.5/6.3%.p=0.018) but mean MMF dose was lower in CSWD: one, three, six, and twelve months in mg-(1970/1831; 1809/1595; 1655/1508; 1604/1414; p<0.017 for each). TAC levels were similar from one to twelve months. Mean white blood cell levels were lower in CSWD at one to twelve months; MMF dose changes for leukopenia were more frequent in CSWD (27/52%,p<0.0001). Cardiovascular risk changes from PTD zero to 365 favored CSWD: mean total cholesterol (mg/dl) (+9.1/-6.7,p =0.014), mean LDL (mg/dl) (+5.2/-6.1 p =0.056), mean HDL (4.5/2.6 p=NS), trigl (+14/-46 mg/dl, p<0.0029), mean weight gain (kg) (5.8/2.1 p=0.042), new onset PTDM requiring insulin (% of pts) (7.2/2.2 p = 0.056). Mean change in Framingham risk points at one year were similar (-2.07/-2.45). Mean Creat were similar at one year (1.51/1.50). The conclusion of the one-year follow-up was that early CSWD compared to CCS provided excellent patient and graft survival, as well as a 6 percent increase in AR, and 4.8 percent increase in moderate AR, and a greater reduction in total and LDL cholesterol, weight gain, and PTDM requiring insulin. The AR increase may be due to lower MMF dosing in CSWD patients.

#1511 A RANDOMIZED, DOUBLE BLINDED, PLACEBO CONTROLLED TRIAL OF EARLY CORTICOSTEROID CESSATION VERSUS CHRONIC CORTICOSTEROID MAINTENANCE THERAPY. E. Steve Woodle, Fujisawa Steroid Withdrawal Study Group. May 24, 2005, 4:40 pm, Calcineurin Minimization/Avoidance (4:00 PM-5:30 PM), 4B.

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Steroid Free Immunosuppression and the Pediatric Renal Transplant Patient

In a similar case-controlled study, the effects of a steroid avoidance protocol in pediatric renal transplant patients on Calculated Creatinine Clearance (CrCl) (Schwartz), Acute Rejection Episodes (ARE), immunosuppressive regimen, and Cytomegalovirus (CMV) infection were studied. From 1999-2004, 14 pediatric patients (age 1-20 years) received transplants without steroids using immunosuppression with Tacrolimus (TAC), Mycophenolate Mofetil (MMF), and Daclizumab (living donor (LD) = 12; deceased donor (DD) = 2). Contemporaneous control patients (N= 24) were matched for donor type (LD vs. DD), age, type of immunosuppression, sex, date of transplant, and original disease. The study compared CrCL, ARE, TAC level, TAC dose in the first 6 months post-transplant and CMV disease in the first year post-transplant. The study found that graft survival at one year was 100 percent in both groups. Mean CrCl of steroid-free versus control patients pts were not different at any time point. There was one ARE in the steroid-free group and two in the control group. There were five episodes of CMV disease in the control group but no episodes in the steroid-free patients. Mean TAC doses (mg/kg) were not different between groups, but TAC levels (ng/ml) at one week were significantly lower in the steroid treated control group, as was the mean level per dose. The conclusion of study found that steroid-free immunosuppresion with TAC, MMF, and Daclizumab provided outcomes that were at least equivalent to steroid based regimens in the first 6 months post transplant.
#1328 IS STEROID FREE IMMUNOSUPPRESSION SAFE FOR THE PEDIATRIC RENAL TRANSPLANT PATIENT? A CASE CONTROL STUDY. Nihar Bhakta, Pornpimol Rianthavorn, David Gjertson, Jennifer Marik, H.Albin Gritsch, Robert Ettenger. May 24, 2005, 12:30 pm, Poster session: Pediatric Kidney Transplantation (12:30 PM-2:00 PM), Hall 4F.

Tacrolimus (TAC) Based Steroid Free Immunosuppression in African-American Recipients of Cadaver Kidneys

The benefits of TAC-based steroid-free immunosuppression were further demonstrated in a controlled study presented at ATC. The study evaluated efficacy and advantages of TAC based steroid-free therapy in 100 cadaver kidney recipients; 50 African-American recipients versus 50 non African-American recipients. Two doses of methylprednisolone (MP) were given on days zero and one and then totally discontinued. Induction was basiliximab and maintenance was TAC and MMF or SLR. Biopsy proven AR was treated with MP and non responders by Thymoglobulin. Serial biopsies were completed to evaluate subclinical acute rejection (SCAR) and chronic allograft nephropathy (CAN). Primary end point was clinical AR and secondary was patient or graft loss. Adverse effects monitored included PTDM, blood lipids and HTN. The study found that tacrolimus-based steroid-free immunosuppression resulted in ≤4% PTDM in both groups. Equivalent AR, and patient and graft survival at two years in cadaver kidney recipients in both African-American and non African-American groups was recorded.
#514 TACROLIMUS (TAC) BASED STEROID FREE IMMUNOSUPPRESSION IN AFRICAN AMERICAN (AA) RECIPIENTS OF CADAVER KIDNEYS (CAD) PROVIDES EQUIVALENT RESULTS COMPARED TO NON AA GROUP. Mysore S. Anil Kumar, Michael Heifets, Michael J. Moritz, Miten H. Parikh, Muhammad I. Saeed, Billie Fyfe, Aparna Kumar. May 22, 2005, 4:20 pm, Steroid Withdrawal/Avoidance (4:00 PM-5:30 PM), 4B.

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About Prograf®

Prograf® is indicated for the prophylaxis of organ rejection in patients receiving kidney or liver transplant and has been marketed in North America, Europe and Japan. Worldwide, Prograf® is commercially available in 68 countries. Currently approximately 70% of new kidney transplant recipients take Prograf®. Only experienced physicians and qualified facilities should mange patients prescribed Prograf®. Increased susceptibility to infection and the possible development of lymphoma may result from immunosuppression. Insulin dependent post transplant diabetes occurred in up to 20% of patients but was reversible in some patients. Black and Hispanic kidney transplant patients were at an increased risk. Common adverse reactions are nephrotoxicity, neurotoxicity, gastrointestinal disturbances, hypertension and infection. Prograf® is contraindicated in patients with a hypersensitivity to tacrolimus. Prograf® injection is contraindicated in patients with a hypersensitivity to castor oil. For full prescribing information, visit www.prograf.com or contact Astellas at 1-800-727-7003. Visit www.transplantlife.com for free educational information related to transplantation.

About Astellas

Astellas Pharma US, Inc. is a subsidiary of Astellas Pharma Inc., located in Tokyo, a pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. In April 2005, the company was formed through the merger of Fujisawa Pharmaceutical Co., Ltd. and Yamanouchi Pharmaceutical Co., Ltd. The organization is committed to becoming a global mega pharmaceutical company by combining outstanding R&D and marketing capabilities and continuing to grow in the world pharmaceutical market.

*Zenapax is a registered U.S. trademark of Hoffmann-La Roche Inc.

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