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1640 MULTI-CENTER, OPEN-LABEL, PROSPECTIVE, RANDOMIZED, PARALLEL GROUP STUDY INVESTIGATING AN EVEROLIMUS-BASED CNI-FREE REGIMEN IN COMPARISON TO A CYCLOSPORINE-BASED STANDARD THERAPY IN DE NOVO RENAL TRANSPLANT PATIENTS (ZEUS STUDY)

K. Budde[1], J. Klempnauer[2], W. Arns[3], C. Sommerer[4], P. Reinke[5], U. Eisenberger[6], W. Fischer[7], S. Kramer[7], F. Pietruck[8]

[1]Nephrology, Charité, Berlin, Germany, [2]Department of Visceral and Transplantation Surgery, Hannover Medical School, Hannover, Germany, [3]Cologne General Hospital, Merheim Medical Centre, Cologne, Germany, [4]Department of Nephrology, University Hospital, Heidelberg, Germany, [5]Department of Nephrology and Internal Intensive Care, Campus Virchow Clinic, Charité University Medicine, Berlin, Germany, [6]Department of Nephrology and Hypertension, University Hospital of Bern, Switzerland, [7]Novartis, Nuernberg, Germany, [8]Department of Nephrology, University Hospital, School of Medicine, Essen, Germany

The ultimate aim of immunosuppressive therapy in transplantation is to provide an efficacious regimen while minimizing non-immune toxicities. By combining synergistic drugs, it may be possible to reduce the exposure to individual agents and therefore avoid adverse effects whilst maintaining favorable clinical outcomes. Until now, no therapy has been recognized as being efficient in the prevention of long-term allograft loss due to chronic allograft dysfunction (CAD) reflecting an unmet medical need in transplantation. Therefore, the use of antiproliferative drugs like Everolimus in combination with the withdrawal of CNI has become an interesting concept in treating calcineurin inhibitor toxicity leading to chronic slow deterioration of renal allograft function.

Therefore, the purpose of the here presented ZEUS study was to assess whether an Everolimus-based CNI-free regimen is as safe and well-tolerated as the Cyclosporine-based standard regimen but results in a better renal function. This 1-year, prospective, open-label, randomized, parallel group, controlled study compared the efficacy, safety and tolerability of an immunosuppressive regimen with Everolimus and EC-MPS to that of Cyclosporine (CsA) and EC-MPS in renal allograft recipients.

The study population consisted of a representative group of 300 de novo kidney transplant recipients. For the first 4.5 months post transplantation, all patients were treated with Basiliximab as induction therapy, CsA, EC-MPS and corticosteroids. 4.5 months post-transplant patients were randomized 1:1 to either a) (n=150) continue the current regimen of CsA and EC-MPS (720mg BID) or b) (n=150) to convert from CsA to Everolimus over a 4 week period and continue with Everolimus (adjusted according to trough levels of 6-10 ng/ml) and EC-MPS (720mg BID). Corticosteroids were prescribed according to center practice with a minimum dose of 5 mg/day. The efficacy of the two treatment arms was assessed by the determination of Glomerular Filtration Rate (GFR), calculated according to Nankivell-method (primary endpoint), Cockcroft-Gault method, and MDRD method. Serum creatinine and slope of creatinine and rejection episodes (treated and biopsy proven), graft loss, death, lost to follow up, as well as treatment failure as a composite endpoint. The patients will be followed-up for safety and graft survival for additional 4 years. At the ICTS we will present the data on the primary and secondary endpoints, safety and efficacy of 285 randomized patients.

In summary, the ZEUS study results are adequate for investigating the influence of different immunosuppressive regimens with or without CNI on short- and long-term renal function. Our data – which will be presented at ICTS - will contribute to the knowledge about CNI-free regimens in renal transplantation. Furthermore, the study will shead some light to the important question about the time point of switching the immunosuppressive regimen from a CNI-based to a CNI-free therapy.

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1641 EFFICACY AND SAFETY OF EVEROLIMUS WITH LOW DOSE CYCLOSPORINE A COMPARED WITH MYCOPHENOLATE MOFETIL AND FULL DOSE CYCLOSPORINE A IN DE NOVO RENAL TRANSPLANT RECIPIENTS

G. Miserlis, V. Papanikolaou, G. Vergoulas, N. Antoniadis, I. Fouzas, D. Vrochidis, A. Papagiannis, G. Imvrios, D. Giakoustidis, D. Takoudas

Organ Transplant Unit,Hippokration General Hospital, Thessaloniki, Greece

Proliferation signal inhibitors (mTOR inhibitors) are used in combination with calcineurin inhibitors for acute rejection prophylaxis and prevention of chronic rejection in renal transplantation.

The purpose of the study was to evaluate and compare the efficacy and safety of two different immunosuppressive protocols (Group A: steroids, everolimus, reduced dose CsA, basiliximab vs. Group B: steroids, MMF, full dose CsA, basiliximab) in de novo renal transplant recipients (RTR).

The analysis included 74 RTR (Group A: 33 pts, Group B: 41 pts) transplanted between January 2005 and March 2007. Recipients and donors mean age were 44.5 and 57.8 years respectively. Sixteen patients (48.5%) from group A and 27 pts (65.9%) from group B had received the kidney allograft from deceased donors. Everolimus and CsA starting dose in group A were 2mg/d and 2mg/KgBW/d while MMF and CsA dose in group B were 2g/d and 5mg/KgBW/d respectively. The mean (±SD) GFR was higher in group A than in group B patients (60.3±14.7 vs 51.3±15.8 ml/min/1.73m2 ,$p<0.05$) six months post transplantation. There was not noticed any significant difference of GFR between the two groups 1 and 12 months after transplantation. Serum creatinine and urine albumin did not differ significantly between the two groups 1, 6 and 12 months post transplantation. Total and LDL cholesterol were statistically significant increased in RTR on immunosuppressive regimen with everolimus at 6 and 12 months after transplantation. (T-cholesterol of group A, 6 and 12 months post transplantation: 278.48±70.98mg/dl and 259.29±84.67mg/dl vs T-cholesterol of group B: 217.37±76.39mg/dl and 202.6±59.21mg/dl, $p<0.05$ and LDL of group A, 6 and 12 months post transplantation: 187.66±56.97mg/dl and 178.47±50.31mg/dl vs LDL of group B: 131.39±35.58mg/dl and 126.18±30.54mg/dl, $p<0.05$). The incidence of biopsy proven acute rejection (BPAR) was 12.1% (4 pts) in group A vs 22% (9pts) in group B. CMV infection occurred in 3 RTR of group A and in 5 of group B. Everolimus trough levels ranged from 3.35 to 9.18ng/ml in group A. CsA dose was reduced by 27.5% and 31.3% at 12 and 18 months post transplantation in group A and this was resulted in reduction of CsA C2 levels by 38.21% and 45.5% at the same time intervals. In conclusion, although mTOR inhibitors are associated with several class specific adverse reactions (hyperlipidemia), concentration-controlled everolimus therapy of de novo renal transplant recipients provide effective protection against rejection with good renal allograft function when used in combination with reduced dose CsA, steroids and basiliximab.

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1642 EARLY DIAGNOSIS OF HEPATIC ARTERY THROMBOSIS AFTER LIVER TRANSPLANTATION WITH AN ICG-CLEARANCE NON-INVASIVE TECHNIQUE

F. Saliba, E. Levesque, S. Benhamida, P. Ichaï, D. Azoulay, R. Adam, D. Castaing, D. Samuel

Hopital Paul Brousse, Centre Hépato-Biliaire, Université Paris Sud, Unité INSERM N°785, Villejuif-FRANCE

Hepatic artery thrombosis (HAT) is a life threatening complication that occurred in 2 to 12% of liver transplant recipients. The diagnostic performance of Doppler-ultrasonography (D-US) is reported to be excellent with 91% sensitivity. False positive results, i.e. non-visualization of flow, are considered to be a limitation of this exam and an angiography or a CT angio-scan is usually required.

Methods Indocyanine green clearance (Cl-ICG) is used to measure the hepatic function and the hepatic blood flow. Recently, with the LiMON® system, the Plasma Disappearance Rate of Indocyanine Green (PDR-ICG) assessment is available by a non-invasive pulse-densitometric method. Serial daily D-US and PDR-ICG measurements were performed after liver transplantation. For each measurement, 0.25 mg/Kg of ICG was given through a peripheral vein.

In a routine screening of 72 liver transplant recipients for PDR-ICG (299