

## A noninferiority, randomized controlled trial of late conversion to once-daily regimen of sirolimus and extended-release tacrolimus versus mycophenolic acid and extended-release tacrolimus for kidney transplant recipients

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**Background:** Once daily regimen could improve medical adherence and quality of life. Sirolimus based regimen can reduce calcineurin inhibitor (CNI) exposure. Therefore, we conducted randomized controlled trial, comparing once daily regimen of sirolimus and extended-release tacrolimus (ER-Tac) versus standard regimen of mycophenolic acid (MPA) and ER-Tac for late conversion in low immunologic risk kidney transplant recipients.

**Methods:** This randomized controlled, open label, noninferiority trial was conducted from April 2018 to March 2022 at King Chulalongkorn Memorial Hospital and Bhumirajanagarindra Kidney Institute Hospital, Thailand. The kidney transplant recipients greater than 4-month posttransplant were randomized 2:1 to once daily arm and standard arm. Patients were followed up for 12 months. The primary outcome was estimated glomerular filtration rate (eGFR), CKD-EPI at 12 months. The noninferiority margin was 5 mL/min/1.73 m<sup>2</sup>. Donor specific antibody and protocol kidney biopsy were followed up at 12 months.

**Results:** Seventy-two kidney transplant recipients were randomized to once daily arm (n=48) or standard arm (n=24). The baseline characteristics of patients were comparable both groups. The primary endpoint, mean eGFR at 12 months was 74.75 mL/min/1.73 m<sup>2</sup> in once daily group and 70.5 mL/min/1.73 m<sup>2</sup> in standard group (difference, 4.24; 95% confidence interval, -4.35 to 12.83). Once daily arm was noninferior as the difference does not exceed noninferiority margin. Mean change eGFR (standard error) at 12-month from baseline of once daily arm and standard arm were 1.97 (1.27) mL/min/1.73 m<sup>2</sup> (P=0.127) and -0.08 (1.69) mL/min/1.73 m<sup>2</sup> (P=0.962), respectively. De novo donor specific antibody incidence rate was 2.1% and 8.3% for once daily and standard groups, respectively.

**Conclusions:** Once daily regimen of sirolimus and ER-Tac was noninferior to standard regimen for mean eGFR at 12-month after conversion in low immunologic risk kidney transplant recipients. Once daily regimen of sirolimus and ER-Tac could be an alternative regimen for low immunologic risk kidney transplant recipients.

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