中文題目：附加 Aliskiren 對治療慢性腎臟病達標的效益

英文題目：Effects of Addition of Aliskiren on Goal Attainment in Chronic Kidney Disease

作　　者：吳孟泰[1]董石城[2]許國泰[1]李建德[1]

服務單位：高雄長庚紀念醫院　腎臟科[1] 新陳代謝科[2]

Background: Aliskiren is recently introduced and becomes the first oral drug to be proved for clinical use in hypertension in the class of direct renin inhibitor. The combination of aliskiren and angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blocker (ARB) in chronic kidney disease (CKD) is controversial, with pro from AVOID Study and con from ALTITUDE. Besides, most of the studies conducted so far were limited to early stage nephropathy with mild to moderate proteinuria. Whether such dual renin-angiotensin-aldosterone system blockade can safely and effectively apply to patients with CKD at various stages and proteinuria status has been uncertain.

Materials and Methods: This is an open-label single-arm study performed in one nephrology out-patient department. We added aliskiren at a dose of 150 mg/day for 6 months in 103 Chinese CKD patients who had taken ACEi or ARB for more than 6 months and still had UPCR > 200 mg/g or systolic blood pressure >130 mm Hg or diastolic blood pressure >80 mm Hg. At 0, 3, and 6 months, mean arterial pressure (MAP), serum creatinine, estimated glomerular filtration rate (eGFR), potassium, and spot urine protein-creatinine ratio (UPCR) were measured and compared with baseline. The primary end point was change in degree of proteinuria. Secondary end points were change in blood pressure, renal function as evaluated with eGFR, and serum potassium level. Factors that might affect the therapeutic response, including change in proteinuria, MAP, and eGFR, were analyzed. All serial data were compared by means of a general linear model for repeated measures, followed by generalized estimating equation. A p-value < 0.05 is considered statistically significant.

Results: Male accounted for 53% of study subjects; their mean age was 63.4 ± 13.0 years old; mean eGFR was 37.4 ± 24.4 mL/min/1.73m^2. The proportion of CKD from stage 1 to 5 was 5%, 10%, 40%, 25%, and 20% respectively. Baseline UPCR was 896 mg/g (95% confidence interval, 701 - 1046 mg/g). Among enrolled patients, 91% had hypertension, 41% had diabetes, 43% had hyperuricemia, and 62% had

hyperlipidemia. At 3 months, the mean UPCR declined to 835 mg/g (583 – 1196 mg/g), a 7% reduction; by the end of the 6-month study period, UPCR was further reduced to 689 mg/g (529 – 897 mg/g), a 23 % reduction from baseline (p=0.001). Besides, one quarter of patients (32 subjects) had over 50% reduction in UPCR at 6 months. The mean eGFR at 3 and 6 months were 35.0 ± 24.2 and 32.8 ± 19.9 mL/min/1.73m^2 and there was no significant change compared with baseline (p=0.708). MAP was reduced by 4.3 ± 13.2 mm Hg at 3 months and 7.9 ± 13.8 mm Hg at 6 months (p<0.001). No participant was withdrawn during 6-months study period due to intolerable adverse events. Four subjects had an eGFR decline of over 30% from baseline at the end of study, while another four subjects' eGFR increased over 30%. Serum potassium level showed an insignificant change during study period at 3 and 6 months (p= 0.314). Three subjects developed hyperkalemia at 3 months, and seven subjects at 6 months; all were in CKD stage 4 or 5, were asymptomatic and continued their medications with adding polystyrene sulfonate to normalize serum potassium. There was no report of symptomatic hypotension, stroke, or death. Both univariate and multivariate analysis showed that neither the proteinuria reduction rate nor the eGFR decline rate during treatment were affected by age, sex, body mass index, the status of diabetic, hypertension, hyperuricemia, hyperlipidemia, the magnitude of basal eGFR, basal MAP, basal proteinuria, or change in MAP from baseline to 6 months. After adjusted for MAP change, UPCR reduction remains unaffected and remarkable (p=0.02).

Conclusion: In the present study, we show a favorable effect of the combination of aliskiren and ACEi or ARB on residual proteinuria and blood pressure reduction irrespective of CKD stages and kidney damage etiologies, after patients have been treated by ACEi or ARB for more than 6 months. It suggests that the therapeutic response to aliskiren add-on in CKD is beyond diabetic nephropathy and regardless of the magnitude of proteinuria and renal function. There is non-significant decline in eGFR or increase in serum potassium level throughout the study period, while infrequent incidences of hyperkalemia in advanced CKD stage merit clinicians' surveillance.