# Linagliptin Alleviates Renal Injury in a Model of Type 2 Diabetic Nephropathy

Session Saturday General Poster Session

General Poster Sessions
Number 563-P | Saturday, June 6, 2015 at 11:30 AM – 1:30 PM | Location: Hall B - Poster Hall
Category Complications–Nephropathy–Basic and Experimental Science

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Dipeptidyl peptidase (DPP)-4 inhibitors offer new opportunities for the treatment of type 2 diabetes. The ability of these agents to attenuate renal fibrosis and retard progression of diabetic nephropathy was suggested recently. In this study we examined the long-term effects of DPP-4 inhibitor linagliptin on structural changes in the kidneys in db/db mice, a model of type 2 diabetes.

Eight-week-old male diabetic db/db mice (BKS.Cg-Dock7$^{m}$+/+Lepr$^{db}$/J) were treated with linagliptin (10 mg/kg per day by gavage) or vehicle for 8 weeks. Renal structural changes were analyzed quantitatively from the light and electron microscopic images.

Linagliptin-treated mice as compared to vehicle-treated animals demonstrated attenuated mesangial expansion estimated by fractional mesangial volume (median 37.4% and 31.0% respectively, $p=0.03$). Glomerular basement membrane and podocyte foot process width was reduced in linagliptin group significantly (both $p<0.01$). The number of podocyte foot processes was increased ($p=0.007$), and the number of endothelial fenestrae in glomerular capillaries tended to be increased ($p=0.1$) on linagliptin treatment. The width of basal membrane of the proximal tubules was diminished by linagliptin significantly ($p=0.007$ respectively).

The data from the current study demonstrate that DPP-4 inhibitor linagliptin ameliorates renal fibrosis and podocyte injury in a model of type 2 diabetic nephropathy.

Keywords DPP-4 inhibitor, Diabetic nephropathy