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**][A3863] Effects of the Phosphate Binder Renagel® (Sevelamer) on Biochemical Parameters and Bone Histology in a Chronic Renal Failure (CRF) Rat Model.**

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**Session Info:** Poster Session: Treatment (10:00 AM - 12:00 PM) Poster Board Number: T1-0872

La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub> and Renagel® have recently been proposed as new phosphate binders. Whilst the effects of Renagel® on bone in CRF have not been studied so far, preliminary studies showed that high La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub> doses (up to 2000 mg/kg/day) may lead to osteomalacia (OM) in CRF rats, and not in NRF animals. While phosphatemia did not differ significantly, a dose-dependent decrease in phosphaturia was noted. To clarify whether the observed OM was a direct effect of La, or occurred because of a phosphate-deficiency, the current pilot-study was set up, in which the effects were compared with those of a non metal-containing, non-absorbed phosphate binder. Twenty male wistar rats (age 14 weeks) underwent a 5/6 nephrectomy. After stabilisation of the CRF, animals were dosed with either 500 mg/kg/day or 1000 mg/kg/day of Renagel® or 1000 mg/kg/day of La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub> for 12 weeks. Serum phosphate showed no statistically significant differences. Phosphaturia showed a clear decrease over time in all treatment groups, reaching significance vs. the vehicle group after 2 weeks in the La group, after 6 and 8 weeks in the high- and low-dose Renagel® groups. Serum PTH did not differ significantly over time in whole groups but individual animals did occasionally show a clear increase in serum PTH. Bone histology revealed a tendency towards an increase in osteoid area, and decrease in bone formation rate in all treatment groups, which was dose-dependent in the Renagel® treated animals. Because of the limited number of animals however, statistical significance was not reached. The effects of Renagel® on bone in CRF appear to be similar to those previously observed with high La<sub>2</sub>(CO<sub>3</sub>)<sub>3</sub> doses. This finding supports our hypothesis that the observed osteomalacia is caused by a phosphate deficiency due to the high doses of phosphate binder, rather than by a direct effect of either phosphate binder on the bone. Furthermore, these results demonstrate that in this animal model, phosphate depletion can occur despite normal serum phosphorus levels.

**Keywords:** Lanthanum; Bone histomorphometry; Renagel