MP-06.17

Efficacy and safety of dutasteride, tamsulosin and the combination in Asian men: 4-year results from the randomised, double-blind, CombAT trial

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Introduction and objective: CombAT investigated the efficacy of dutasteride/tamsulosin combination *versus* both monotherapies for improving symptoms and clinical outcome in men with moderate-to-severe BPH.
Materials and Methods: In this international, randomised, double-blind, parallel-group study, men ≥50 years with BPH (IPSS ≥12, total prostate volume [PV] ≥30 cc, serum PSA 1.5–10 ng/mL, Q_{max} 5m–15 mL/s) received dutasteride 0.5 mg/day, tamsulosin 0.4mg/day, or the combination for 4 years. The 4-year primary endpoint was rate of AUR or BPH-related surgery; secondary endpoints included clinical progression rate (one of: IPSS deterioration ≥4 points, BPH-related AUR, incontinence, renal insufficiency or recurrent UTI), change from baseline in IPSS, PV, Q_{max}, and BPH impact index (BII). Although CombAT was not powered to detect treatment differences in subpopulations, Asian men represented a large subgroup (n=325), and a *post-hoc* analysis of the 4-year CombAT data for Asian men is presented.
Results: At 4 years, the proportion of subjects with AUR or surgery was 6.5% for combination, 1.9% for dutasteride, and 10.7% for tamsulosin. There was a trend for less clinical progression with combination (18.7%) *versus* tamsulosin (33.0%, p=0.016), but not *versus* dutasteride (17.9%). Mean change in IPSS from baseline was significantly greater with combination (-6.4) *versus* tamsulosin (-2.3; p<0.001), but not *versus* dutasteride (-4.9, p=0.14). Mean change in PV was significantly greater with combination (-13.3 cc, -29.9%) *versus* tamsulosin (+3.6 cc, +0.7%; p<0.001) but, as expected, not different to dutasteride (-12.8 cc, -30.2%). Significant improvement in BII was observed with combination (-2.6) *versus* tamsulosin (-0.9; p<0.001) but not *versus* dutasteride (-2.1). Incidence of adverse events (AEs) was similar with combination (89%), dutasteride (82%) and tamsulosin (88%). Drug-related AEs were more common with combination (32%) *versus* dutasteride (11%) or tamsulosin (18%). Rates of withdrawal due to any AE were similar (9%, 12%, 8%, respectively).
Conclusions: Combination treatment provided significantly superior and sustained improvements in symptoms, flow rate, and quality of life *versus* tamsulosin monotherapy in Asian men, in line with results in the overall population. Reduction in AUR/surgery risk with combination *versus* tamsulosin was in line with the overall population, although larger numbers would be needed to achieve statistical significance.

Moderated Poster Session 7: Stones 1
Monday, November 2
15:15-16:45

MP-07.01

Renal Histological Changes after Roux-En-Y Gastric Bypass Surgery in a Diet Induced Obese Rat Model

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Introduction and Objective: Roux-en-Y gastric bypass (RYGB) surgery is the most common surgical intervention for long-term weight loss in morbidly obese patients. As popularity and demand for this therapy has expanded, renal manifestations such as oxalate nephropathy and nephrolithiasis appear to be increasing in this patient population. With the intention to develop a murine model of bariatric surgery induced calcium oxalate nephrolithiasis, we performed RYGB in obese rats on a high fat, normal oxalate diet and tested whether the RYGB surgery causes detrimental renal injury and mineral deposition.
Materials and Methods: Sprague-Dawley rats, fed a high-lard diet to induce gross obesity, were randomized to RYGB (n=6), GI-intact sham-operated obese controls (Controls, n=4), or GI-intact sham-operated obese pair-fed rats (PF, n=8). Daily body weight and food intake were recorded for 40 days. Food efficiency was calculated. Rats were sacrificed and renal tissue was obtained for protein and immunohistochemical analysis. Stained sections were imaged using an imaging microscope and image-analysis software (Axioplan 4.1). Osteopontin (OPN) stain was estimated based on percentage of stained area compared to the kidney section size. ED-1 (macrophage-derived mononuclear cell stain) was estimated on the number of counted cells in each field divided by the number of fields examined. Data were compared using ANOVA and t-test.
Results: RYGB vs. PF control rats had significant reductions in body weight and food efficiency (p<0.001) and significantly greater renal tubule mineralization and basophilia, patchy interstitial nephritis, and glomerular changes by H&E staining. The inner medulla of the RYGB rats stained stronger for osteopontin (70% vs. 43%, p=0.01) while the outer medulla of the RYGB rats stained stronger for ED-1 (39 cells/10x field vs. 11 cells/10x field, p=0.05).
Conclusions: In this rat model, RYGB surgery is associated with significant weight loss, decreased food efficiency, renal mineral deposition, and insidious, chronic renal interstitial cellular damage. Osteopontin is up-regulated within the tubular lumen and urinary space, likely due to oxalate mineralization. ED-1 positive cells are attracted to the interstitium around the thin loop of Henle, suggesting that the injurious mechanisms provoked by mineralization involve not only inflammation but also antigen presentation and fibrogenesis.

MP-07.02

Taurine Protects the Kidney from Oxidative Injury by the Mitochondrial-Linked Pathway in a Rat Model of Calcium Oxalate Nephrolithisis

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Introduction and Objective: Hyperoxaluria and crystal deposition induce oxidative stress (OS) in kidney; both mitochondria and NADPH oxidase were considered to be the source of reactive oxygen species (ROS). Taurine is known as an antioxidant. We investigate the putative source of ROS, as well as the effects of taurine treatment on renal protection in a rat model of calcium oxalate nephrolithisis.