

[2011] [THU0027] BCX4208, A NOVEL URATE-LOWERING THERAPY, WAS GENERALLY SAFE AND WELL TOLERATED IN TWO 3-WEEK STUDIES IN GOUT SUBJECTS

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Background: BCX4208 is a Purine Nucleoside Phosphorylase (PNP) inhibitor, which represents a new class of drug that blocks the generation of precursors of uric acid at a higher level in the metabolic pathway than xanthine oxidase inhibitors. BCX4208 lowered uric acid as demonstrated in 2 short term efficacy studies; BCX4208-201 evaluated the serum uric acid (sUA)-lowering effects of 40 - 240 mg/day oral BCX4208 administered as monotherapy for 21 days, and BCX4208-202 evaluated the dose response relationship on sUA when administered at 20 – 80 mg/day for 21 days as monotherapy and in combination with allopurinol, 100 - 300 mg/day.

Objectives: To describe the safety profile of short term BCX4208 use.

Methods: Safety data from studies 4208-201 and 4208-202 were combined and summarized by BCX4208 dose, with subset analysis by BCX 4208 dose for each allopurinol level (placebo, 100mg, 200mg, and 300mg). All BCX4208 dose groups were combined and analyzed in total and by dose.

Results: These 2 randomized trials had a combined safety population (received BCX4208 or placebo) of 186, 141 who received BCX4208 (92 alone and 49 with one of 3 doses of allopurinol) and 45 who received placebo. Colchicine 0.6 mg/d or naproxen 250 mg twice daily was used for gout flare prophylaxis in both studies. Demographics were well balanced between the BCX4208 and placebo treated subjects. Mean age was 49 (range 23-69); 97% were male, 67% white, 10% black, and 8% Hispanic. The mean (range) body mass index (BMI) was 34.5 (22.2-62.9) and mean (range) sUA at enrollment was 9.8 mg/dl (8-15mg/dl). Adverse events (AEs) occurred in 59% of subjects receiving BCX4208 and 62% of the placebo group. There were no AE differences in frequency or severity in the subjects receiving concomitant allopurinol and those only receiving BCX4208. Only 1 serious AE occurred, a hemorrhoidal bleed in a BCX4208-treated subject not attributed to study drug. The most common AEs reported in subjects receiving BCX4208 were diarrhea (10%), headache (10%), peripheral edema (6%), lymphocyte count decreased (6%), and URI (5%). AE frequency and severity were similar in the placebo and BCX4208 groups, except for peripheral edema and lymphocyte count decrease. Two subjects (4%) receiving placebo and 7 subjects (5%) receiving BCX4208 (with and without allopurinol) discontinued therapy due to an AE. All reported AEs in BCX4208-treated subjects were mild or moderate with the exception of 1 report each of severe diarrhea and severe diverticulitis. Four subjects receiving placebo experienced 7 severe AEs. There were no opportunistic infections reported, nor was there an imbalance in overall infection rate reported between BCX4208 and placebo treated subjects. Effects on lymphocytes were dose related. A total of 2.1% of subjects experienced a decrease of 1 grade or more in absolute lymphocyte count.

Conclusions: BCX4208 was safe and well tolerated when administered at doses up to 240 mg/day for 21 days. The addition of BCX4208 to allopurinol did not alter the safety profile. The frequency of diarrhea may be explained by the high rate of colchicine use (77%). Long term efficacy and safety of BCX4208 is currently being evaluated at doses of 5 – 40 mg/day in combination with allopurinol.

Disclosure of Interest: S. Dobo Employee of: BioCryst Pharmaceuticals, Inc., A. Flynt Consultant for: BioCryst Pharmaceuticals, Inc., A. Hollister Employee of: BioCryst Pharmaceuticals, Inc., W. Sheridan Shareholder of: BioCryst Pharmaceuticals, Inc., Employee of: BioCryst Pharmaceuticals, Inc.

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Bone diseases other than osteoporosis, metabolic diseases and crystal diseases