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A PHASE 2 STUDY IN WOMEN WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME (IC/BPS) OF THE NOVEL P2X3 ANTAGONIST AF-219

Hypothesis / aims of study

P2X3 purinoceptors drive sensitization of bladder sensory neurons in response to ATP, causing chronic symptoms of pain, discomfort and urgency. Furthermore, P2X3 knock-out mice displayed bladder hyporeflexia and P2X3 inhibition suppresses visceral hyperalgesia in rodent models. Based upon these findings, our hypothesis was that a P2X3 antagonist, AF-219, would reduce interstitial cystitis/ bladder pain syndrome (IC/BPS) symptoms.

Study design, materials and methods

This was a randomized, double-blind, placebo controlled study in women with IC/BPS with moderate to severe pain. The objective was to determine the efficacy (pain scores) and safety of treatment with AF-219 or placebo for 4-weeks. Urinary urgency, micturition frequency and Global Response Assessment (GRA) were also assessed. The study incorporated a titration design, introduced as a result of poor gustatory tolerability seen with commencement at higher doses. AF-219 or Placebo was started at 50 mg BID and titrated up by 50 mg BID every day until 300 mg or until the highest tolerable dose. Women aged 18-80 years of age who had the diagnosis of IC/BPS for more than 6 months and moderate to severe pain measured by the mean daily Numeric Pain Rating Scale (NPRS) were entered into the study. Cystoscopy was performed either at time of diagnosis or prior to randomization.

Results

There were 36 women treated with AF-219 and 38 women treated with Placebo under the titration protocol. 50% of AF-219 treated patients received a final dose of at least 250 mg BID and 18% of Placebo-treated patients did not reach the maximum dose. At 4-weeks there was a decrease in the NPRS in AF-219 treated patients from 6.2 at baseline to 3.3 compared to 6.5 to 4.5 in Placebo-treated patients. There was a similar reduction in the Worst Pain, GUPI, Urinary Urgency and GRA at week 4. There were 5 patients with Hunner Lesions on cystoscopy. 3 of the 4 patients treated with AF-219 with Hunner lesions had a > 1 point reduction on the NPRS and 2 of 4 had a > 5 point reduction at week 4. The 1 placebo treated patient had a 0.9 point reduction in the NPRS at week 4. Patients reported no SAEs and AEs were generally mild. The most frequent reported AE in AF-219 treated patients was dysgeusia/hypogeusia.

Interpretation of results

Patients treated with AF-219 had improvement in the key symptoms of IC/BPS: pain scores, urinary urgency and general improvement in patient reported symptoms. AF-219 was generally well tolerated after titration was implemented in the study.

Concluding message

Based on the results of this study there should be further evaluation of AF-219 in patients with IC/BPS

Disclosures

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