

Long-term safety of an NSAID with built-in gastroprotection for treatment of pain and inflammation related to OA and RA: comparative results from blinded and open-label one- year safety trials of a single-tablet combination of ibuprofen-famotidine

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Purpose

Gastrointestinal (GI) toxicity is an issue with long-term NSAID use. Adherence with co-prescribed GI protective therapies is often suboptimal and associated with reduced functional efficacy. Double-dose H₂ receptor antagonists provide benefit in decreasing NSAID-associated upper GI injury (Cochrane review). HZT-501 (DUEXIS) [single-tablet formulation of ibuprofen 800 mg and famotidine 26.6 mg tid; total daily dose of 2400mg ibuprofen and 80 mg famotidine] was shown previously to significantly reduce endoscopic upper GI ulcers at 6 months as compared to ibuprofen 800 mg tid alone (two randomized double blind trials: REDUCE-1 and REDUCE-2).

Method

Assessment of long-term safety of HZT-501 (up to 12 months [mos] of treatment [tx]) for patients (patients) with OA, RA or moderate pain). Studies enrolled patients 40 to 80 years expected to require daily NSAID therapy for >12 mos with no history of ulcer or active GI complications, cardiac, renal and/or hepatic disease. Patients were allowed to continue on concomitant low-dose aspirin/anticoagulant (LDA/OAC) therapy. *Trial 1* enrolled patients who completed either REDUCE-1 or REDUCE-2 which required baseline absence of ulcers. Patients completing 24 weeks blinded tx (no ulcer; continue requiring daily NSAIDs) were eligible for follow-on trial for an additional 28 weeks of double-blind tx assignment. Crossover between txs was not allowed. *Trial 2*, open label safety trial, HZT-501 tid up to one year. For both studies, endoscopies were performed only if indicated, data included serious adverse events (SAEs), tx emergent adverse events (TEAEs), clinical laboratory assessments, vital signs, and physical exams.

Results

Trial 1 - Of 179 patients enrolled, 132 received HZT-501 (112 completed) and 47 received IBU (38 completed). TEAEs incidence was comparable in both groups for the one year period. There were no clinically relevant differences between tx groups in vital signs, hematology, biochemistry values or physical exams. Twenty-six patients on LDA therapy enrolled in the follow-on trial; 20 in the HZT-501 arm and 6 in the IBU arm, a ratio of 4.3:1. Of the 26 patients on LDA therapy, 18 completed HZT-501 and 5 completed IBU tx.

Trial 2 – Eighty-six patients enrolled; 40 patients completed one year of tx, 26 patients discontinued prematurely, 20 patients are currently on active tx. Preliminary unaudited safety data is available for 80 of the 86 patients. Eleven of 86 enrolled patients (12.8%) were on concomitant LDA therapy; 4 completed, 5 withdrew early from the trial and 2 have completed at least 30 weeks of tx.

Conclusions

Safety results for HZT-501 are consistent with the known safety profiles of ibuprofen and famotidine used individually. In addition to the previous findings of a significant decrease in upper GI endoscopic ulcers, these results demonstrate that HZT-501 offers a potential new option for patients who require long-term NSAID use.