BACKGROUND

Chronic urticaria (CU) is defined by spontaneous wheals lasting longer than 24 hours and having a persistence of at least 6 weeks. This condition is considered as idiopathic (CIU) if no apparent etiology was considered. It is a common skin condition, with a prevalence of 0.1% to 3% in Europe and in USA. CU can affect the Quality of Life (QoL), primarily as a result of sleep disruption, energy loss, fatigue, social isolation and emotional/sexual disturbances. This condition follows a chronic course with spontaneous remission and relapses for several years. The symptoms of chronic urticaria, include oedema, erythema and pruritus, are primarily associated with histamine release from normal mast cells. Oral H1-receptor inverse agonists (H1 antagonists) are the treatment of choice. According to the EAACI/GA2LEN/EDF guidelines for urticaria management and diagnosis, the new so-naming antihistamines are the first line of treatment for chronic urticaria.

Other mast cell mediators include eosinoids, cytokines, proteases, cytokines and platelet activating factor (PAF) and histamine have mutually complementary activities. Blockade of these mediators is likely to be more effective treatment strategy for chronic urticaria.

POUR THE PURPOSE OF

A responder analysis in chronic idiopathic urticaria (CIU) patients was performed by means of a pooled analysis, in order to strengthen the clinical results obtained in previous trials with rupatadine 10 and 20 mg.

MATERIAL AND METHODS

The pooled data from two randomised, double-blind, placebo-controlled, 4-week multicentre studies were used for this analysis. The first trial was a dose-ranging study comparing the efficacy and safety of rupatadine 5-, 10- and 20 mg once daily or placebo in 248 CIU patients. The second study compared the efficacy of rupatadine 10 and 20 mg, once daily, with placebo in 334 CIU patients.

In both trials, patients were included if they suffered moderate to severe CIU as active CIU (score ≥ 2 labeled as moderate pruritus) for at least 3 days during the week before inclusion, with a total score of active CIU > 6 and documented number of active CIU (urticaria wheals) with or without an associated angioedema for at least three days per week over the last 6 weeks prior to the Screening Visit. Response rates are defined in Table 1. The statistical analysis responder was employed using two logics models. Model 1 extracted effects for study, treatment and study-by-treatment interaction. In the absence of heterogeneity (not significant interaction between study and treatment), the final model model only effects for study and treatment. This model was not found in any of the responder’s analysis. The values of percentage of improvement are shown in tables and figures as raw values, whereas the p value is obtained from the final logistic model.

RESULTS

535 patients were treated with placebo, rupatadine 10 and 20 mg (ITT population). Figures 2, 3 and 4 shows the percentage of patients that obtained a >50%, >75% and LCLM of scores improvement, Mean Pruritus Score (MPS), Mean Total Symptom Score (MTSS, MPS + MTSS) after 28 days; p<.002.

DISCUSSION

CUI treatment is difficult. Eliciting stimuli must be investigated and controlled. Mast cell directed therapy includes corticosteroids, ciclosporin A or phototherapy. Target organ or symptomatic therapy is normally done with H1-receptor antagonists. Because of the good safety profile, second-generation antihistamines are considered the first line symptomatic treatment for chronic urticaria. But there is any consensus on which is the percentage of clinical improvement that we must expect using the recommended dose for each idiopathic in a defined period of time. Most experts agree with the fact that higher dosages should be used as routine. Some others experts recommend to initiate the treatment with the combination of more than one antihistamine (sedative with non sedative). A 50% of symptoms reduction after 28 days of treatment employing low dose of just one antihistamine is considered an adequate improvement.

This responder analysis, at different responses levels, showed that the efficacy of rupatadine 10 and 20 mg, once daily with placebo, in 334 CIU patients showed a higher improvements in all scores with significantly differences in each treatment group.

CONCLUSION

1. The responder analysis ads strengthen to the rupatadine clinical trials results.
2. It would help the clinicians to evaluate the rupatadine response in CIU patients.
3. This study support the need to use higher doses of no sedating antihistamines in chronic urticaria.
4. A complete responder analysis should be considered in order to evaluate antihistamine therapeutic benefits.

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8. Study Placebo Rupatadine 10 mg Rupatadine 20 mg
9. Phase II 69 73 67 209
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11. Total 180 183 175 538
12. Criteria Definition Based on
13. >50% Reduction from baseline Percentage of patients who achieved an improvement of at least 50% from baseline in symptom score of at least 75% from baseline in symptom score.
14. > 75% Reduction from baseline Percentage of patients who achieved an improvement of at least 75% from baseline in symptom score of at least 75% from baseline in symptom score.
15. Reduction greater than those observed Percentage of patients who showed a greater improvement than those observed. Confidencial Interval with least 75% from baseline in placebo group.
16. MPS
17. MTSS
18. MNW

Table 1. Summary of responder criteria

Table 2. Number of patients with CIU included in clinical trials of rupatadine

Fig 1. Chemical structure

Rupatadine is a selective long-lasting histamine H1-receptor inverse agonist, currently authorized in European Community for the treatment of chronic idiopathic urticaria and allergic rhinitis. This drug has shown both antihistamines and anti-PAF effects through its interaction with specific receptors. Other only few others H1 antihistamines showed some marginal anti-PAF effect.