SAFETY PROFILE OF RUPATADINE IN THE TREATMENT OF CHRONIC URTICARIA

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BACKGROUND

Chronic urticaria is defined by spontaneous wheals long-lasting more than six weeks[1]. Conventionally, if any apparent etiology was considered, chronic urticaria is categorized as idiopathic. Chronic idiopathic urticaria (CIU) is a relatively common skin condition. Wheals and pruritus are the most prominent sign and symptom[1]. The symptoms of CIU are mainly associated with dermal mast cells degranulation and histamine release. This fact has led to use inverse agonist H_1 antihistamines to treat the urticarias[2].

Chronic urticaria bleaching requires to control of multiple involved factors and also long periods of continuous treatment. Non-sedating H_1 antihistamines have been recommended by the EAACI / GA²LEN / EDF guideline as first line of treatment[3]. One of the reasons for this kind of recommendation is the good safety profile of these drugs.

Rupatadine is a new selective long-acting histamine H_1 receptor inverse agonist (H_1 antihistamine) which is currently approved as a once daily dose of 10 mg, for the treatment of chronic idiopathic urticaria[5,6] and allergic rhinitis[7].

AIM OR OBJECTIVE

To assess Rupatadine safety profile in moderate to severe Chronic Urticaria without an identifiable aetiology or "Chronic Idiopathic Urticaria" (CIU) treatment.

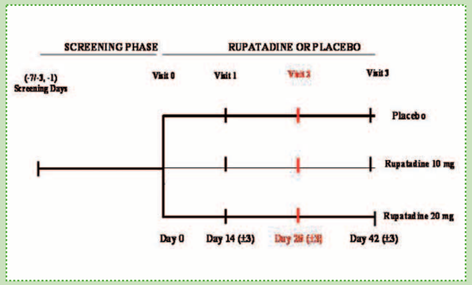
MATERIAL AND METHODS

The pooled data from two randomised, double blind and placebo controlled, 4-week multicentre studies were used for this analysis. The first was a dose-ranging study comparing the efficacy and safety of placebo or rupatadine 5 mg, 10 mg and 20 mg once daily in 283 CIU patients[4]. The second study compared the efficacy of placebo or rupatadine 10 mg and 20 mg once daily in 334 CIU patients[5]. Efficacy and safety profile was evaluated over 6 weeks of treatment.

The incidence and type of adverse events (AEs) was assessed based on the patients' diaries reports, routine laboratory tests results, clinical and physical examinations and ECG, before and at the end of the treatment period. (**Fig. 1**)

Descriptive statistics was applied. Incidence of AE during the 4-weeks was calculated. The qualitative parameters were described by treatment group in terms of frequencies and percentages. The initial comparability of the treatment groups concerning to demographic and anthropometric variables was analyzed, as well as clinical characteristics at the time of inclusion by means of T test, Chi square test or Fisher test according to the type of variable.

Figure 1. Study design



CONCLUSION

All dosages of rupatadine administered once daily during these two clinical trials showed to be safe and well tolerated. Rupatadine can be recommended as first line treatment for moderate-to-severe Chronic Urticaria without an identifiable aetiology.

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RESULTS

Sample demographic data are summarized in **Table I**.

Global incidence of AEs was 28.02% with placebo-treated group (n=182), 32.86% with rupatadine 5mg-treated group (n=70), 30.11% with rupatadine 10 mg-treated group (n=186) and 35.20% with rupatadine 20 mg-treated group (n=179). The 11.54%, 14.29%, 11.83% and 20.67% of the AEs respectively were related with the treatment.

The most frequents reported related AEs were headache 2.75%, 2.86%, 2.69% and 3.91% and somnolence 3.85%, 4.29%, 3.76% and 13.41% for placebo, rupatadine 5mg, rupatadine 10 mg and rupatadine 20 mg, respectively. Any of these AEs forced to discontinue the treatment.

Just somnolence AEs was significantly higher with rupatadine 20 mg than with placebo or rupatadine 10 mg. The others AEs did not show significant differences among the treatment groups. (Fig. 2 and 3)

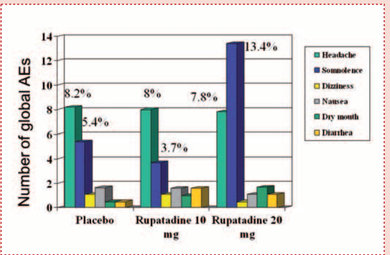
No clinically relevant AEs were observed related with ECG, blood testing and vital signs studies during rupatadine clinical trials. Concerning ECG no relevant findings were reported. Any patient showed a QTc value longer than 470 msec and in any case QTc increased 60 or more msec. One asymptomatic and not clinically relevant CPK increased value was reported as SAE.

Overall headache AE described with 5 mg desloratadine was 15,5% (placebo 10%)[8] and 12,6% (placebo 16,8%)[9]. Other significant AEs observed during desloratadine clinical trials were nausea, dry mouth, fatigue, upper respiratory tract infection or dizziness.

Table I. Pooled CIU Demographic data (ITT population)

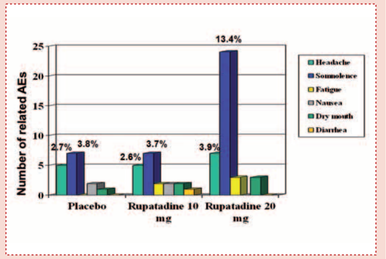
		Treatment				
		Placebo	Rupatadine 5 mg	Rupatadine 10 mg	Rupatadine 20 mg	All
Gender						
Male	**N**	58	19	52	54	183
	%	31.87	27.14	27.96	30.17	29.66
Female	**N**	124	51	134	125	434
	%	68.13	72.86	72.04	69.83	70.34
Age (years)		36.31	39.1	40.1	37.8	38
All	**N**	182	70	186	179	617

Figure 2. Incidence of global adverse events (AE) (n<1, at least one) after 4 weeks treatment



Somnolence: Rupatadine 20 vs. placebo, p<0.001; Rupatadine 20mg vs. Rupatadine 10mg p<0.001
Headache: No differences between treatments

Figure 3. Incidence of related adverse events (AE) (n<1, at least one) after 4-weeks treatment



Somnolence: Rupatadine 20 versus placebo, p<0.001; Rupatadine 20mg versus Rupatadine 10mg p<0.001
Headache: No differences between treatments

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