

THE JOURNAL OF Allergy AND Clinical Immunology

August 1998 • Volume 102 • Number 2

The clinical efficacy of H₁ antagonists in urticaria and rhinitis

- [Previous article](#) in Issue
- [Next article](#) in Issue
- [Drug links](#) from Mosby's DrugConsult
- [Genetic information](#) from OMIM
- Citation of this Article
 - View on [PubMed](#)
 - Download in [citation manager format](#)
 - Download in [Medlars format](#)
- [Related articles](#) in PubMed

To the Editor:

Monroe et al. (J Allergy Clin Immunol 1997;99:S798-S806) state that there is no correlation between the suppressive effect of an H₁ antihistamine on a histamine skin reaction and the clinical efficacy of the same drug in patients with chronic idiopathic urticaria (CIU) and seasonal allergic rhinitis (SAR).

Although cetirizine is obviously more potent than terfenadine and loratadine in controlling the histamine-induced skin reactions, these 3 drugs appear to demonstrate equivalent clinical efficacy in double-blind, placebo-controlled studies performed in CIU and SAR (12 and 31 studies, respectively) as all the *P* values found in these studies are nonsignificant.

This conclusion is one of the most common statistical errors in the interpretation of clinical data.^{1,2} Clinical trials that show no statistically significant difference between treatments do not prove that these treatments are equivalent. The demonstration of equivalent efficacy requires other statistical methods, such as the 2 1-sided procedure proposed by

Schuirman³ compared with the methods mentioned by Monroe et al. Acceptance of the null hypothesis that there is no difference may often be attributed to the low statistical power

of the investigation (inclusion of an insufficient number of patients). None of the 43 double-blind CIU and SAR studies showed statistically significant differences between treatments because none were correctly dimensioned to differentiate active compounds having moderate, but nevertheless real, differences in their respective clinical efficacy.

Indeed, if we assume that the difference in efficacy between the treatments investigated is about 10%, 250 subjects per treatment group should be included in these trials to differentiate these treatments at a level of significance ($P = .05$) with a power of 80% (coefficient of variation, 40%).⁴ The mean total numbers of patients enrolled in the clinical studies reviewed by Monroe et al. in CIU and SAR are 91 (27 to 182) and 228 (53 to 487), respectively, well short of 250 per group.

One might object that a clinical benefit of only 10% for drug A in comparison with drug B is merely borderline or negligible. Such an objection could also be an error. Indeed, if we assume that patients with SAR treated with drug B will have a mean of 10 days without symptoms, whereas they are symptom-free for 11 days with drug A (a difference of 10%), and if we assume that 1 million patients take drug A, this means that the total difference caused by the intake of drug A amounts to 1 million days. In other words, a benefit of 2740 years for drug A. The question then becomes the following: Is it worthwhile?

Jean Pierre Rihoux, MD, FFPM
Fergal Donnelly, MD, MSc
Bernard Burtin, PhD
UCB Pharma S.A.
MDI-Chemin du Foriest
B-1240 Braine-l'Alleud
Belgium
1/8/91751

References

[TOP](#)

1. Note for guidance on statistical principles for clinical trials. ICH Topic E9, Statistical principles for clinical trials. (CPMP/ICH/363/96). London: The European Agency for the Evaluation of Medicinal Products; 1998.
2. Van Houwelingen HC. The future of biostatistics: expecting the unexpected. *Stat Med* 1997;16:2773-84.

MEDLINE

3. Schuirmann DJ. A comparison of two one-sided test procedure and the power approach for assessing the equivalence of average bioavailability. *J Pharmacokinet Biopharm* 1987;15:657-80.

MEDLINE

4. Fleiss JL. The design and analysis of clinical experiments. New York: John Wiley & Sons; 1986.
-