

Cost Effectiveness of Levocetirizine in Chronic Idiopathic Urticaria

A Pooled Analysis of Two Randomised Controlled Trials

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Abstract

Background: Chronic idiopathic urticaria is a distressing condition that severely affects patients' quality of life. The overall costs associated with this disease, both for the healthcare payer and society, are unknown. The objective of this study was to evaluate the cost effectiveness of levocetirizine, a first-line treatment for urticaria.

Methods: Data were collected from two placebo-controlled trials and from official French databases. The effectiveness of the treatment was assessed by the mean number of pruritus-free days experienced by the patient within a 30-day period (PFD₃₀). Direct cost parameters were medications used, medical procedures and hospitalisations for urticaria or treatment of adverse events. Productivity cost parameters were the workdays lost, defined as absenteeism and/or presenteeism, resulting from urticaria. The costing was performed using a French societal perspective. Costs were reported in € (2002 values) and were standardised to a 30-day month. Whenever possible, incremental cost-effectiveness ratios (ICERs) were derived from these data.

Results: The pooled sample contained 294 patients. Compared with placebo, patients in the levocetirizine group experienced an additional mean 6.5 (95% CI 3.8, 9.3) pruritus-free days per month ($p < 0.001$). Considering only direct medical costs, the incremental cost of treatment with levocetirizine was totally offset by the reduction in other medical costs (i.e. reduced cost of additional medications, medical procedures and hospitalisations). From the perspective of society, treatment with levocetirizine was cost saving, with a net gain of €91.93 per patient per month.

Conclusion: Treating chronic idiopathic urticaria with levocetirizine is a dominant strategy for society since it is more effective (in terms of pruritus-free days gained) and less costly than placebo.

Chronic urticaria is a particularly afflictive skin disease, the prevalence of which is estimated to reach 0.75%. It is characterised by almost daily whealing, often associated with angioedema, and lasts for at least 6 weeks.^[1,2] Chronic urticaria greatly impacts the patient's quality of life since many patients report problems attributable to their disease in facets of everyday life including sleep, rest, mobility, occupational, social and recreational activities. Furthermore, it has been suggested that patients with chronic urticaria feel as lacking in energy, socially isolated and emotionally upset as heart disease patients.^[3-5] In chronic idiopathic urticaria (CIU), the daily or almost daily occurrence of wheals and pruritus is highly distressing and has an adverse effect on a patient's quality of life.^[3,6] There is also evidence that patients with CIU may experience a substantial loss in productivity at work, school or daily activities. A 25–30% loss in productivity prior to treatment has been reported in one study.^[6]

The evaluation of costs associated with chronic diseases has a growing role in the allocation of healthcare resources. It is increasingly necessary to consider the cost effectiveness of a given treatment in order to determine the most appropriate use of limited resources. The cost of a disease is comprised of the following components: direct costs, which include medical costs (e.g. costs linked to medications, physician visits or hospitalisations) and non-medical costs (e.g. costs linked to transportation to the hospital to treat the disease) and productivity costs (e.g. associated with loss of productivity and/or social activity).

Antihistamines are the first-line treatment for CIU.^[7] Levocetirizine (Xyzal®, UCB, Braine L'Alleud, Belgium)¹ is a highly selective H₁-receptor antagonist combining potent antihistaminic and anti-inflammatory properties.^[8] The comparative *in vivo* potency of levocetirizine in humans has been

shown to be consistently superior to other newer antihistamines such as desloratadine,^[9-12] fexofenadine^[12-14] and cetirizine.^[12,15] The same is true for its clinical efficacy in direct comparison with desloratadine^[16-18] and fexofenadine.^[19]

An extensive review of the literature in MEDLINE, EMBASE and SciSearch revealed no economic analyses of any drug treatment in CIU; consequently, there were no studies showing the health economic impact of daily levocetirizine treatment in adults with CIU. This is the first paper to address this gap in knowledge by reporting the results of a cost-effectiveness analysis comparing levocetirizine 5mg with placebo in the treatment of CIU.

Methods

The pooled data from two randomised, double-blind, placebo-controlled, 4-week multicentre studies were used for these analyses. The first was a dose-ranging study comparing the efficacy and safety of levocetirizine 2.5mg, 5mg and 10mg once daily in 258 CIU patients randomised to one of the active arms or placebo^[20] (only those patients randomised to receive levocetirizine 5mg daily or placebo were included in the current cost-effectiveness analysis). The second study compared the efficacy of levocetirizine 5mg once daily with placebo in 166 CIU patients.^[21] Both trials followed exactly the same design. One week after the screening visit (i.e. 1-week baseline period), suitable patients were randomised to either placebo or levocetirizine 5mg daily treatment. A control visit was performed 1 week after randomisation. This visit was followed by the end-of-treatment visit 3 weeks later (i.e. a total of 4 weeks' treatment period), and by a final follow-up visit 1 week after the end-of-treatment visit (see figure 1). Besides safety concerns, the primary objective of both trials was to evaluate the effectiveness of daily treatment with levocetirizine

1 The use of trade names is for product identification purposes only and does not imply endorsement.

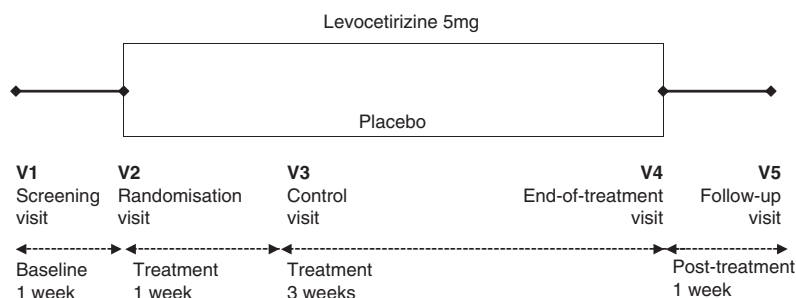


Fig. 1. Schematic representation of the design of the two studies.

5mg tablets versus placebo on pruritus severity in CIU over 4 weeks of treatment.

Patients were included in the studies if they had CIU, i.e. episodes of hives of characteristic wheal and flare appearance, occurring regularly (at least three times a week for a period of at least 6 weeks during the previous 3 months), without an identifiable cause. During the baseline period, patients had to have at least 3 days with moderate or severe pruritus and wheals present in order to be randomised to one of the two treatment groups.^[20,21]

Direct medical and productivity cost parameters, in addition to efficacy and safety parameters, were collected at baseline and during the treatment period.

Effectiveness Parameter

From a health economic point of view, an effectiveness parameter aims to provide an overall picture of the subject's status regarding his or her condition. To date, CIU has not been assessed using a health-economic effectiveness parameter and, therefore, the pruritus-free-day parameter was devised. During both the baseline and the treatment periods, patients had to provide a daily report of pruritus severity over the previous 24 hours, which was scored from 0 to 3 (0 = absent; 1 = present but not disturbing; 2 = disturbing but not hampering daytime activities and/or sleep; 3 = hampering daytime activities and/or sleep). A pruritus-free day was defined as the absence of pruritus over the last 24

hours (score = 0). In order to present the results as clearly and legibly as possible, the number of pruritus-free days (nPFD) during baseline and treatment periods was standardised to 30-day periods (PFD₃₀) according to the following formula:

$$\text{PFD}_{30} = (\text{nPFD} / \text{total evaluated days}) \times 30$$

Direct Cost Parameters

The direct cost parameters were the number of medication events (i.e. each time a new medication was used by the patient), medical procedures and hospitalisations related to CIU or to the study medication's adverse events. The relationship of these events to CIU was determined based on the reason(s) provided by the investigator for requesting these resources. Reasons were coded prior to unblinding with the WHO-ART dictionary. All resources with URTICARIA in their preferred term were selected. All medical resources with an onset date within the baseline or the treatment period were included in the analyses. The number of items used (i.e. number of medication events, medical procedures or hospitalisations) were computed and standardised per 100 patients for ease of comparison between the placebo and levocetirizine groups.

Productivity Cost Parameters

The productivity cost parameters refer to the productivity lost at work and consist of both absenteeism (full days off work) and presenteeism (pro-

ductivity lost while at work) resulting from urticaria. Both were expressed as the mean number of days lost per patient per month. Data for these parameters were collected using the Pharmacoeconomic Indirect Costs (PIC) questionnaire. The PIC questionnaire gathers data on whether a subject was restricted at work because of urticaria, data on absenteeism (number of full days unable to work) and data on presenteeism (the reduction in productivity while at work). Presenteeism was derived by multiplying the number of days with reduced productivity by the level of productivity lost on those days, measured on an 11-point scale (from 0 = not able to perform work/usual daily activities, to 10 = able to perform work/usual daily activities). The PIC questionnaire was previously developed and tested among a group of patients with allergic rhinitis and adapted for use in the urticaria context. Data on the productivity lost over the past month was collected at baseline. Data on productivity lost since the last visit was collected at the two subsequent visits during the treatment period.

Monetary Valuation of the Health Economic Parameters

A French societal perspective was used for all patients regardless of country of origin to assign costs to both direct and productivity cost parameters. Costs were reported in € (2002 values) and, for ease of comparison with effectiveness parameters, were also standardised to a 30-day month. Costs for medication events (including the patient's co-payment) were taken from the package cost reported in the VIDAL (www.vidalab.net). Other unit costs were found on official websites, namely www.le-pmsi.org (a diagnosis-related group [DRG]-based system) for hospitalisation, www.ameli.fr (the general website of the French health insurance) for tests and physician visits, and www.insee.fr for productivity costs.^[22] The monthly cost of levocetirizine treatment (30 tablets) was an addi-

tional cost incurred in the levocetirizine group. Based on the human capital approach,^[23] the unit cost for productivity loss per working day was derived from the mean 2002 gross monthly salary for private and semi-public enterprises, divided by the number of usual working days per month. Each non-working patient was assigned a €0 cost for productivity.

The incremental cost-effectiveness ratio (ICER) per pruritus-free day was determined by calculating the difference in average costs as a proportion of the difference in average effectiveness of levocetirizine 5mg versus placebo, according to the following formula:

$$\text{ICER} = \frac{\text{cost}_{\text{levocetirizine}} - \text{cost}_{\text{placebo}}}{\text{effectiveness}_{\text{levocetirizine}} - \text{effectiveness}_{\text{placebo}}}$$

The ICER provides information on the cost and the effectiveness of the outcomes associated with changing from one treatment to another, i.e. from no treatment (placebo) to levocetirizine 5mg treatment.

Statistical Analysis

The relevance of pooling the trials was assessed by evaluating the differences between the studies regarding sociodemographic characteristics and severity of the disease at baseline. Except for sex distribution, the differences observed in age, employment status and pruritus score at baseline were not statistically different between the two trials (Chi-square p-values >0.05) [table I and table II]. Given the small clinical relevance of the differences observed between the trials, their data were pooled without any adjustment for subsequent analysis.

All analyses were performed using SAS® System software and on the intention-to-treat (ITT) population, with the exception of the productivity cost parameters (i.e. number of days lost), which were reported for the working ITT population. The mean PFD_{30s} over the treatment period were compared between groups using an ANCOVA on the rank^[25] with PFD₃₀ over baseline as covariate and treatment

Table I. Baseline characteristics of the 294 patients enrolled in the two studies (148 placebo-treated and 146 levocetirizine-treated patients)

Patients' baseline characteristics	Study 1 ^[20]	Study 2 ^[21]
No. of patients in the ITT population	128	166
placebo group	63	85
levocetirizine 5mg group	65	81
Country (no. of patients)		
France	128	
Switzerland		30
Germany		136
Sex (%)		
men	33	41
women	67	59
Mean age (y)	42.2	42
Working status [no. (%)]		
full, partial, other employment	79 (62)	109 (66)
no employment	49 (38)	57 (34)

ITT = intention-to treat.

as factor. Rank ANCOVA is a nonparametric approach to analysis of covariance (ANCOVA) problems that is useful when the hypotheses of linearity, conditional normality and homogeneity of variances and of regression slopes are suspect.^[25] In order to account for the difference between the placebo and the levocetirizine groups in the number of medication events at baseline (see Results section for the figures), the mean number of medication events over the treatment period was compared between groups using a Poisson regression model with treatment as factor and the number of medication

events at baseline as a covariate. For the productivity cost parameters, a variance stabilised bootstrap-t method was used to compare the mean number of workdays lost between treatment groups at baseline and over the treatment period, and to compare the change in mean number of workdays lost from baseline. Inference regarding the mean costs associated with lost productivity in the two treatment groups was also provided by the non-conventional bootstrap-t technique because of the skewness of the cost distribution.^[26] A Bayesian bootstrap was used to generate the 2000 samples for these analyses.^[27] The

Table II. Mean pruritus severity score evaluated over the previous 24 hours during the baseline and treatment periods for each study^[20,21,24]

Period	Treatment group	Mean pruritus severity score (SD) ^a	Difference vs placebo (95% CI)	p-Value ^b
Study 1				
Baseline	Placebo	2.3 (0.5)		
	Levocetirizine 5mg	2.1 (0.5)		
Treatment	Placebo	1.8 (0.1)		
	Levocetirizine 5mg	0.9 (0.1)	0.9 (0.6, 1.2)	<0.001
Study 2				
Baseline	Placebo	2.1 (0.6)		
	Levocetirizine 5mg	2.1 (0.6)		
Treatment	Placebo	1.5 (0.1)		
	Levocetirizine 5mg	0.9 (0.1)	0.6 (0.4, 0.9)	<0.001

a The scale used for pruritus over the previous 24 hours is: 0 = absent; 1 = present but not disturbing; 2 = disturbing but not hampering daytime activities and/or sleep; 3 = hampering daytime activities and/or sleep.

b p-Value obtained from an ANCOVA with baseline score as covariate and treatment as factor.

CI of the ICER were determined using a non-parametric bootstrap analysis with 2000 bootstrap replications.^[28,29]

Results

Patients' characteristics at baseline in each study are presented in table I. In total, the pooled sample contained 294 patients, of whom 63% were female, with a mean age of 42 years, and 64% of the patients were working (fully or partially). Furthermore, the results of each study regarding their primary objective (i.e. pruritus severity in CIU over the 4 weeks of treatment) are reported in table II. In both studies, statistically significant improvements were observed in the pruritus severity score for the levocetirizine 5mg group compared with the placebo group over the 4-week treatment period.

Effectiveness Parameter

The mean number of pruritus-free days per month (PFD₃₀) per treatment group is presented in figure 2. The mean PFD₃₀ was higher in the levocetirizine group than in the placebo group both at baseline and during the treatment period. However, only the between-group difference observed over the treatment period was statistically significant ($p < 0.001$). An additional 6.5 PFD₃₀s (95% CI 3.8, 9.3)

were gained in the levocetirizine group compared with the placebo group.

Direct Cost Parameters

The placebo group had a mean number of medication events of 1.4 (95% CI 0.0, 2.7) per 100 patients over the baseline period that increased to 35.4 (95% CI 28.7, 42.2) over the treatment period. The mean number of medication events in the levocetirizine group increased from 2.1 (95% CI 0.4, 3.7) during baseline to 2.7 (95% CI 0.9, 4.5) over the treatment period. Therefore, the number of medication events over the treatment period was more than ten times lower in the levocetirizine 5mg group than in the placebo group ($p < 0.001$), although it was significantly higher for the levocetirizine group than the placebo group at baseline ($p = 0.05$). Antihistamines for systemic use constituted the majority of additional medications for urticaria used in all treatment groups (100% in the levocetirizine and 78.8% in the placebo group). Furthermore, in the placebo group, systemic corticosteroids (5.8%), psycholeptics (antipsychotics, hypnotics, sedatives, anxiolytics) [5.8%] and psychoanaleptics (antidepressants, psychostimulants, nootropics) [3.8%] were frequently reported. Medical procedures for urticaria were only reported in the placebo group. When standardised to 100 patients, this corresponded to 0.67 medical procedures per 100 patients for placebo and none for levocetirizine over the treatment period. Similarly, only one 4-day hospitalisation was reported in the placebo group while no hospitalisations for urticaria were reported in the levocetirizine group. This corresponded to 2.7 hospitalisation days per 100 patients for placebo compared with zero for the levocetirizine group over the treatment period. Because of the small numbers of procedures and hospitalisations, no statistical comparisons between the treatment groups were made.

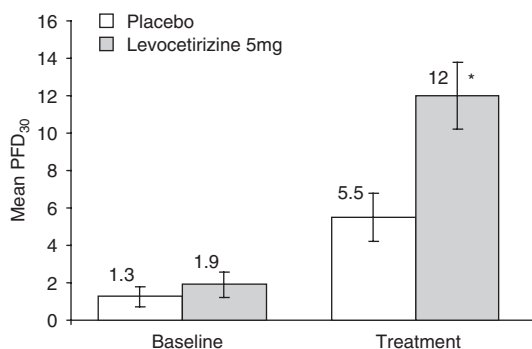


Fig. 2. Mean pruritus-free days per month (PFD₃₀) in the placebo and levocetirizine 5mg groups, with 95% CIs (pooled data). Means over the treatment period are adjusted for baseline using an ANCOVA model. * $p < 0.001$ vs placebo.

Table III. Mean number of workdays lost per patient per month (95% CI) in the intention-to-treat working population

	Baseline period		Treatment period		Change from baseline ^a	
	placebo (n = 92)	levocetirizine (n = 96)	placebo (n = 92)	levocetirizine (n = 96)	placebo (n = 92)	levocetirizine (n = 96)
Absenteeism	0.93 (0.39, 1.99)	0.76 (0.28, 1.55)	1.36 (0.51, 2.50)	0.66 (0.19, 1.49)	0.33 (-0.78, 1.62)	-0.08 (-0.83, 0.68)
Presenteeism	0.43 (0.19, 0.81)	0.73 (0.36, 1.36)	1.02 (0.54, 1.69)	0.41 (0.15, 0.92)	0.71 ^b (0.10, 1.53)	-0.31 (-0.72, 0.01)
Overall productivity loss ^c	1.18 (0.49, 2.33)	1.37 (0.68, 2.41)	2.24 (1.18, 3.51)	0.71 ^d (0.28, 1.57)	1.03 (-0.33, 2.51)	-0.40 (-1.19, 0.19)

- a Mean changes do not equal the difference between treatment and baseline periods because of the exclusion of missing data. Negative values indicate a reduction in workdays lost, i.e. an increase in productivity. Positive values indicate an increase in workdays lost, i.e. a decrease in productivity.
- b Mean change from baseline different from 0: p-value from a variance stabilised bootstrap-t method <0.05.
- c The sum of mean absenteeism and mean presenteeism does not add up to the mean overall productivity loss because of the exclusion of missing data for the computation of each parameter (absenteeism, presenteeism and overall productivity lost).
- d p-Value from a variance stabilised bootstrap-t method for the comparison with the placebo group <0.05.

Productivity Cost Parameters

Results of the mean number of workdays lost because of urticaria at baseline and over the treatment period (table III) show that the work loss as a result of CIU was substantial. No statistically significant difference between groups in work productivity lost at baseline was observed. Up to 31.1% of the patients in the placebo group experienced productivity loss over the treatment period for a mean of 2.24 days per patient. These numbers were significantly reduced in the levocetirizine group.

Patients receiving levocetirizine had a lower overall mean productivity loss (p < 0.05) than the placebo group over the treatment period. Absenteeism and presenteeism were also lower for the levocetirizine group versus placebo, but these differences did not reach statistical significance. From the analysis of the change from baseline in the number of workdays lost, it appeared that there was an increase for the placebo group (change >0 corresponding to a reduction in productivity, statistically significant for presenteeism) while there was a marginal decrease in the levocetirizine group (change <0, not statistically significant).

Monetary Valuation of the Health Economic Parameters

In the absence of levocetirizine treatment (i.e. placebo group), the monthly cost of CIU reached €177.36 per patient per month (table IV). Productivity costs accounted for >90% of this total cost.

Considering only direct medical costs, table IV also shows that the incremental cost of treatment with levocetirizine is totally offset by the reduction in other medical cost categories (i.e. additional medications, medical procedures and hospitalisations). However, in comparison with placebo, treating CIU patients with levocetirizine did not significantly reduce the total direct medical costs (i.e. net

Table IV. Mean costs in the placebo and levocetirizine groups over the treatment period for the total intention-to-treat population

	Mean costs [€ per patient per month] (95% CI) ^a		
	placebo (n = 148)	levocetirizine (n = 146)	incremental cost ^b
Levocetirizine	0	13.20	13.20
Additional medication	2.16 (1.56, 2.85)	0.25 (0.09, 0.50)	-1.92 ^c (-2.64, -1.29)
Medical procedure and hospitalisation	11.66 (0.55, 44.81)	0.00 (0.00, 0.00)	-11.66 ^c (-44.91, -0.71)
Total direct costs	13.82 (2.61, 48.86)	13.45 (13.29, 13.70)	-0.37 (-37.04, 10.71)
Absenteeism	96.39 (46.03, 173.53)	44.48 (12.22, 98.81)	-51.92 (-139.87, 28.40)
Presenteeism	67.15 (36.64, 108.16)	27.51 (11.21, 60.54)	-39.64 (-90.00, 2.45)
Total productivity costs	163.54 (97.44, 244.74)	71.99 (33.63, 133.58)	-91.55^c (-185.84, 3.71)
Total direct and productivity costs	177.36 (109.88, 263.22)	85.43 (47.04, 147.05)	-91.93^c (-188.48, -0.68)

a The 95% CI was calculated using a Bayesian variance stabilised bootstrap-t method.

b A negative cost difference indicates that the cost for the levocetirizine group is lower than the cost for the placebo group.

c p-Value from a Bayesian variance stabilised bootstrap-t method <0.05.

gain of €0.37 per patient per month; 95% CI -37.04, 10.71; $p = 0.97$).

When productivity costs were taken into account, treatment with levocetirizine was cost saving, with a total net gain of €91.93 (95% CI 188.48, 0.68) per patient per month compared with placebo ($p < 0.05$; table IV and figure 3).

Incremental Cost-Effectiveness Ratio

In comparison with placebo, treatment with levocetirizine showed improved effectiveness (i.e. mean PFD₃₀) and generated significant savings from the perspective of society (including both di-

rect medical and indirect costs) but not for the healthcare payer (including only direct medical costs). For society, treating CIU patients with levocetirizine is thus a dominant strategy compared with placebo. The robustness of these findings was assessed by generating 2000 bootstrap replications of the cost and effectiveness estimates. From the perspective of healthcare payers, only 39.9% of the bootstrap replications lay within the dominant quadrant of the cost-effectiveness plane. However, only 2.5% of the samples presented an ICER above €1.75 per PFD₃₀ (figure 4). From the perspective of society, results were much more robust since as many as 98.4% of the bootstrap samples lay within the dominant quadrant (figure 5).

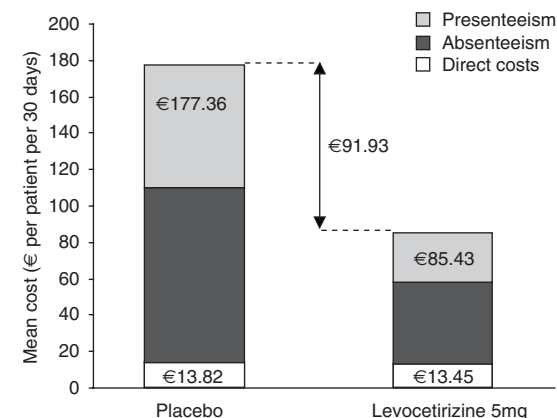


Fig. 3. Mean costs (€ per patient per 30 days) in the placebo and levocetirizine 5mg groups over the treatment period – total intention-to-treat population.

Discussion

The objective of treating patients is to relieve their distress. The measure of effectiveness for this analysis, i.e. the mean number of pruritus-free days (PFD₃₀) assesses whether this aim was reached. The analysis shows clearly that 1 month of treatment with levocetirizine increased the number of pruritus-free days by 6.5 days compared with placebo treatment. This is a clinically highly relevant result since a primary goal of CIU treatment is to alleviate the pruritus experienced by patients with CIU. This is in line with the superior potency of levocetirizine in

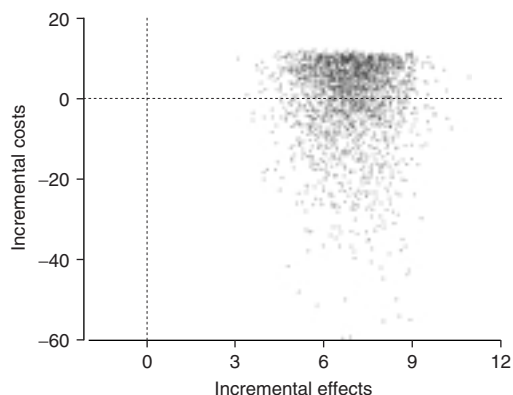


Fig. 4. Cost-effectiveness plane (healthcare payers' perspective) with 2000 incremental cost-effectiveness ratio (ICER) bootstrap replications of levocetirizine 5mg versus placebo – intention-to-treat population. Incremental costs are the additional direct costs; incremental effects are the additional pruritus-free days.

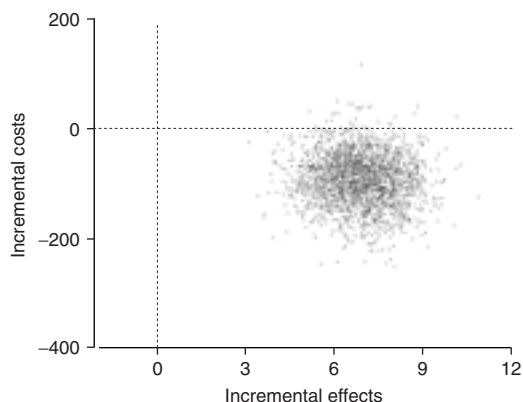


Fig. 5. Cost-effectiveness plane (societal perspective) with 2000 incremental cost-effectiveness ratio (ICER) bootstrap replications of levocetirizine 5mg versus placebo – intention-to-treat population. Incremental costs are the additional direct and productivity costs; incremental effects are the additional pruritus-free days.

treating wheal, flare and itch, as shown in various comparative trials with other newer antihistamines like desloratadine^[9,10,12] and fexofenadine.^[12,13]

The results of the direct and productivity cost analyses provided evidence that CIU patients receiving treatment with levocetirizine show a better overall cost profile than those in the placebo group. This was mainly manifested by reduced productivity costs in the levocetirizine group, in comparison with

the placebo group, which incurred much higher absenteeism and presenteeism costs. Together with other social improvements, such as a better quality of life^[30] (which was, however, not quantified in the current investigation), this illustrates the fact that societal benefits can surely be derived from treating CIU patients with levocetirizine.

Physicians are accustomed to considering direct medical costs when making decisions about treatment, while taking productivity costs (e.g. absence at work) into consideration may not seem very obvious, and may seem even unrealistic. However, productivity costs should also be considered if the aim is to assess the cost from a societal perspective. In this study direct medical costs were not significantly lower in the levocetirizine group compared with the placebo group. However, inclusion of both direct medical and indirect costs resulted in a significant net benefit of €91.93 per month per patient treated with levocetirizine in comparison with placebo-treated patients ($p < 0.05$). Therefore, not only does levocetirizine treatment effectively relieve the symptoms of CIU patients, but it also saves money for society as a whole because CIU patients do not need additional medications or hospitalisations, and because they can spend more time working and at a higher level of productivity.

Limitations to this analysis exist. Firstly, data were collected from two clinical trials. The resulting careful medical follow-up of the patients may thus lead to a reduction in the severity of complications, as well as an increase in the placebo effect. The differences observed in the trials may therefore underestimate those observed in real life. Another limitation is the use of French costing for all patients. However, since urticaria treatment is similar across European countries, the medical resources used are not expected to differ substantially. Similarly, no differences were observed across countries in the degree of productivity loss reported at baseline. Thirdly, the time horizon of the investigation was

limited to 4 weeks. Although a longer term horizon would have been more desirable, the major health and economic outcomes have certainly been captured within the current time-frame. Fourthly, levocetirizine treatment was compared with placebo instead of existing therapies. This is because only placebo-controlled data for CIU were available; no comparative studies of levocetirizine versus other antihistamines have been performed. Finally, productivity changes were measured by the human capital method, which, although a pragmatic method, may not be the most appropriate one. Indeed, it has been argued that this method may overestimate the true cost to society if losses in production could be compensated by the worker on his return or by his colleagues (i.e. the so-called friction cost methods). Those transaction costs have not been considered here.

The current investigation found that, from a societal perspective, treatment with levocetirizine is a dominant strategy in comparison with placebo. This result is very robust since >98% of the bootstrap ICER replications were found to be in the dominant quadrant of the cost-effectiveness plane. However, extrapolation of the current findings to the general French population, i.e. at the macroeconomic level, should only be performed with great caution since the controlled environment in which cost and outcomes data have been collected may not reflect regular practice in real-world settings.

As there are currently no other published economic evaluations of urticaria treatments, it is not possible to compare the results obtained here with those of other studies. However, an ICER of US\$5 per symptom-free day (1989 values) has been suggested as the upper limit for an asthma treatment to be considered as cost-effective versus an alternative treatment.^[31] If a similar ceiling ratio is applied to the cost of a pruritus-free day for urticaria, then treatment with levocetirizine is highly cost-effective versus placebo since all bootstrap ICER replications

were <€5 per pruritus-free day. This is true both for the societal perspective (i.e. considering direct and indirect costs) and for the healthcare payers (i.e. with direct medical costs alone).

Conclusion

Treating CIU with levocetirizine is dominant over placebo, i.e. it increases the number of pruritus-free days and leads to cost savings for society.

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