



Original Article

A study on the subjective compliance and acceptance of oral lansoprazole in traumatology. The ECOFT-TR Study

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ABSTRACT

Objective: To assess compliance with oral lansoprazole disintegrating tablets (LODT) in patients treated by traumatology specialists.

Material and method: A multicenter, observational, cross-sectional study involving 370 traumatology specialists and patients aged 18 or more. Study logistics were sponsored by Almirall Laboratories, S.A.; neither investigators nor patients received any economic compensation for their participation. Patient subjective compliance with LODT was assessed with the Haynes Sackett test. Acceptability was based on patients global assessments of the drug organoleptic characteristics and properties of use, and preferences regarding previous treatments, recorded by means of a self-administered 15-item ad hoc questionnaire with a 2-5-point Likert-type scale, that patients fulfilled once.

Results: One thousand and eighty five patients were analyzed for the main endpoint. Mean age was 56.09 (13.8) years; 56.77% were women. Mean treatment duration was 51.24 (38.8) days. 94.74% of the patients complied with the treatment. Mean percentage of compliance was 94.5 (12.12); 91.09% of patients rated the treatment as "acceptable or highly acceptable." No significant differences were observed between compliant and non-compliant patients in terms of demographic or clinical variables. Mean percentage of compliance was significantly higher among patients without concomitant illness or treatment and without difficulties in taking tablets. One non-serious adverse reaction was reported in one (0.09%) patient.

Conclusions: Compliance with lansoprazole orally disintegrating tablets was high. Patients reported that this formulation improved their compliance and that they preferred LODT to previous medication. Tolerability was excellent.

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Estudio sobre el cumplimiento subjetivo y la aceptabilidad de lansoprazol comprimidos bucodispersables en traumatología. Estudio ECOFT-TR

RESUMEN

Objetivo: Valorar el cumplimiento terapéutico con lansoprazol, comprimidos bucodispersables, en pacientes tratados por especialistas en traumatología.

Material y método: Estudio observacional, transversal. Participaron 370 especialistas en traumatología que incluyeron a pacientes con un mínimo de 18 años. Los aspectos logísticos del estudio fueron financiados por Laboratorios Almirall, S.A.; los investigadores y pacientes no percibieron compensación alguna por su participación en el estudio. La valoración subjetiva del cumplimiento con lansoprazol comprimidos

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bucodispersables se realiz o mediante el test de Haynes-Sackett. La aceptabilidad del tratamiento, considerada como la valoraci n general del paciente tras evaluar las caracter sticas organol pticas y propiedades de uso, y su preferencia con respecto a tratamientos previos, se evalu o mediante un cuestionario ad hoc, autoaplicado, de 15  tems con una escala tipo Likert con 2-5 posibles respuestas, que los pacientes cumplieron en una  nica ocasi n.

Resultados: Fueron valorables 1.085 pacientes, con una media \pm desviaci n est ndar de edad de $56,09 \pm 13,8$ a os; un 56,77% eran mujeres. La media de tiempo en tratamiento fue $51,24 \pm 38,8$ d as. El 94,74% de los pacientes cumplieron con el tratamiento. El grado medio de cumplimiento fue $94,5 \pm 12,12$. El 91,09% de los pacientes calific o el tratamiento como «muy aceptable/aceptable». No hubo diferencias significativas en el porcentaje de pacientes cumplidores seg n las variables demogr ficas y cl nicas. El grado o porcentaje de cumplimiento fue significativamente mejor entre los pacientes sin enfermedades y tratamientos concomitantes y sin dificultad en la toma de comprimidos. Para 1 (0,09%) paciente se notific o una reacci n adversa no grave.

Conclusiones: El cumplimiento con lansoprazol comprimidos bucodispersables fue muy elevado. Los pacientes valoraron que la formulaci n bucodispersable de lansoprazol les ayudaba a cumplir mejor con el tratamiento y lo prefirieron al que recib an previamente. La tolerabilidad fue excelente.

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Introduction

Lansoprazole is a potent proton pump inhibitor (PPI) whose mechanism of action is the specific inhibition of the final phase of acid secretion in the parietal gastric cell, independent of the type of stimuli that led to the increase in secretion (histaminergic, cholinergic, or gastrinergic).¹ Of the numerous PPI currently on the market, lansoprazole is the one that possesses a greater availability (80%–90%) after the first dose; produces an inhibition of gastric secretion in a rapid and effective manner, and leads to rapid symptomatic improvement.² Lansoprazole has shown to be effective and well tolerated for the prevention of gastric ulcer induced by non-steroidal anti-inflammatory drugs (NSAID) and the treatment of gastric ulcers related to SAID in patients who require treatment maintained in a constant manner.³

Lack of pharmacologic treatment compliance goes from 7 to 65% according to the type of drug and the disease present, and leads to a poor control of the latter. Lack of compliance is increased in the case of chronic diseases, which is associated with an increase in morbidity and mortality.⁴ It has been shown that, in patients undergoing chronic treatments, there is a higher risk that treatment compliance is reduced with time.⁵ With respect to treatment with lansoprazole, in spite of the fact that capsules are widely accepted by the patients,⁶ following the prescription can be affected in geriatric and pediatric patients, as well as patients with swallowing problems or simply because access to liquids outside their home might be difficult.^{7,8}

The drug characteristics, such as the size of the pills, the texture, shape and taste, have been pointed out as those aspects that generate a larger deal of complaints on the part of the patients.⁷ Later studies on the acceptance of oral forms of different treatments have confirmed these observations.^{9–13} Therefore, it has been demonstrated that the acceptance of an oral treatment, based on a positive evaluation by the patient on its taste, shape, texture, appearance and ease for swallowing characteristics, determines the preference of one form of administration over another^{9–14} and, in consequence, implicates an increase in treatment compliance and clinical improvement.^{15–17}

The new oral formulations of drugs offer a substantial benefit with respect to capsules, because their increased ease in administration can lead to larger compliance with the established treatment.⁷ An example of this is mirtazapine, an antidepressant drug, whose oral form was preferred by 38% of the patients versus 12% who preferred capsules.¹⁸

Because of the relevance of this aspect and taking into account the bioequivalence in terms of efficacy and safety of oral lansoprazole,¹⁹ the present study had, as objectives, to evaluate the subjective compliance with oral lansoprazole treatment in the common clinical traumatology practice, a specialty that use as a large amount of these treatments, and to determine whether said compliance was related to the acceptance of the drug on the part of the patients.

Material and methods

After authorization, an observational, transversal, and multicentric study was designed, carried out in the common clinical practice conditions of the researchers, specialists in the area of traumatology. Logistical aspects of the study were financed by Almirall Laboratories; researchers and patients did not receive any compensation for their participation in the study.

Patients included had a minimal age of 18 years who had been prescribed oral lansoprazole according to common clinical practice for the prevention of gastric ulcers related to the use of NSAID at least 28 days before inclusion into the study. Excluded patients had alterations in the sense of taste or smell, severe kidney failure (creatinine clearance <30 mL/min) and/or incapacity to understand and answer the study questionnaire, as well as pregnant or breastfeeding patients.

The initial calculation of the sample size was done parting from the hypothesis of maximum indetermination, according to which prevalence was estimated at 50% of compliant patients, with a 95% confidence interval, a maximum approximate precision of 2.8% and estimating approximately 20% of patient loss due to omission or lack of response. Under these a priori assumptions, the participation of approximately 1500 patients was determined as necessary in order to have 1225 valid patients. Finally, of the 1111 recruited patients, 1085 were subject to evaluation, leading to an approximate precision of 3%. Therefore, the number of patients included resulted sufficient to guarantee the validity of data. Calculations were done using a PASS 2002 software package.²⁰

The main variable was treatment compliance, evaluated through the self-communicated Haynes-Sackett compliance test,^{21,22} which is divided into 2 parts (Figure 1). In first place, the patients are asked if he or she have any difficulty taking pills in a general way. To that end, they are explained the difficulty patients have when taking medication; the following phrase is employed: “Most of the patients have difficulty taking all of their pills.” Then they are asked “Do you encounter any problems taking yours?” In second place the patient

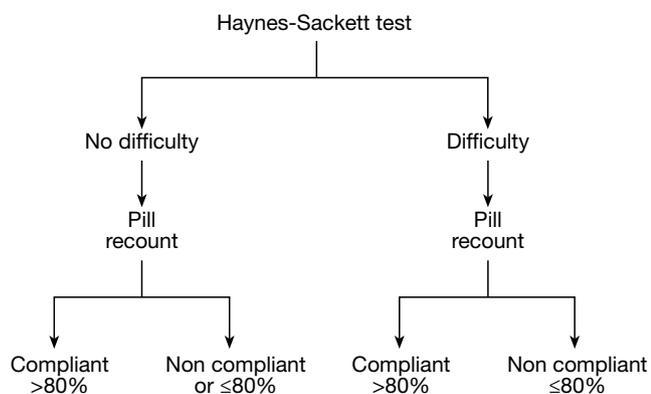


Figure 1. Haynes-Sackett test algorithm for the evaluation of compliance.

is asked on pills taken during the month prior with the following question: "in the past 28 days, how many Opiren® Flas pills do you think you might not have taken?" In relation to this data, the percentage of compliance (PC) is calculated, on a scale from 0 to 100, according to the following formula: $PC = \frac{\text{total number of pills presumably consumed}}{\text{total number of pills that should have been consumed}} \times 100$.

Patients were considered as compliant when they manifested taking more than 80% of medication in the 4 weeks prior, according to the corresponding questions on the Haynes-Sackett test.

To guarantee interview homogeneity, the questions and instructions were included in the questionnaire booklet and the researchers were instructed to follow what had been specified in an exact manner.

Secondary variables evaluated were acceptance and patient preference for treatment with oral lansoprazole with respect to previous treatment. In order to do that, an ad hoc, self-applied questionnaire with 15 items of a Likert scale type with 2 to 5 answer options was designed and with patients completing it only once. The evaluation of the patients on the degree of patient acceptance of treatment with oral lansoprazole was performed after the evaluation of the different organoleptic characteristics (size, taste, taste intensity, aftertaste, speed of dissolution) and properties of the drug (ease and comfort of use in taking the drug). The questionnaire also included patient perception on whether the drug helped them to better comply with treatment, as well as possible preference over previous treatments. Patients completed the questionnaires without intervention by the researcher.

Finally, tolerance was evaluated using a spontaneous notification registry for suspicious adverse events related to the oral formulation of lansoprazole.

All of the surveys were individually reviewed and data was introduced in a database created for such an end which had safety margins and internal coherence norms, after which those cases with anomalous or incoherent values were reviewed. To guarantee data trustworthiness a validation before and after entering data was performed through a data analysis plan in which filters and validations performed were specified a priori.

Statistical analysis was performed with the SPSS version 12.0.1 support package. For the descriptive analysis of the demographic and clinical characteristics of the patients and their treatment, as well as for the distribution of the response to the different organoleptic characteristics and properties of use of oral lansoprazole, means, standard deviation and interval for qualitative variables, as well as frequency and percentage for qualitative variables was estimated. For the analysis of the main study variable, treatment compliance, the 95% confidence interval (95% CI) was also estimated, and its

relationship with gender, age, diseases and concomitant treatments as well as patient perception of the difficulty patients have taking pills, was also estimated using the χ^2 test.

The study was approved by the Clinical Research Ethics Committee of the Teknon Medical Center of Barcelona. All of the patients gave their informed consent before being included, according to the Helsinki convention.

Results

Three-hundred seventy traumatology specialists participated, recruiting a total 1111 patients. Of these, 1085 (97.66%) were considered for the analysis.

Table 1 describes the demographic characteristics of the patients. Mean time of oral lansoprazole treatment at the moment of inclusion was 51.24 (38.8) days. Figure 2 shows the total percentage of compliant patients and Table 2 describes the percentages per group of patients. No statistically significant differences in the percentage of compliant patients was seen in relation to gender, age, concomitant disease or treatment, difficulty for taking pills and degree of acceptance.

Table 3 describes the degree or percentage of compliance, calculated from the number of pills taken in the 28 days prior, for patients in general and for groups of patients. This analysis observed a degree of compliance, which was significantly higher in patients without diseases and concomitant treatments and without difficulty taking pills ($P < .001$).

Table 4 describes the evaluation of patients on the different organoleptic characteristics and Table 5 relates to properties of use and subjective perception of compliance. After evaluating the different organoleptic characteristics and the ease and comfort of use of the pills, 91.09% determined that treatment was acceptable or very acceptable (Figure 3). With relation to preference, 94.81% of patients who had taken prior treatments ($n=565$) indicated that they preferred oral lansoprazole.

With respect to tolerance a non-serious adverse event was notified, which corresponded to a slight tingling of the tongue for a single patient (0.09%).

Discussion

The objective of this study was to determine compliance of treatment with oral lansoprazole and prove whether this compliance could be related to the acceptance of this drug on the part of the

Table 1
Demographic characteristics of the patients ($n=1085$)

	n	(%) ^{b,c}
Gender ^a		
Male	463	(43.23)
Female	608	(56.77)
	Mean	SD
Age, years ^a	56.09	13.8
	n	(%) ^c
Age by category:		
Between 18 and 35 years	74	(6.94)
Between 35 and 54 years	386	(36.12)
Between 55 and 74 years	525	(48.97)
Older than 74 years	81	(7.6)

Abbreviations: SD, standard deviation.

^a In 14 patients, gender was not specified and in 19 patients, age was not specified.

^b Percentage calculated on the total number of patients who indicated gender ($n=1071$).

^c Percentage calculated on the total number of patients who indicated age ($n=1066$).

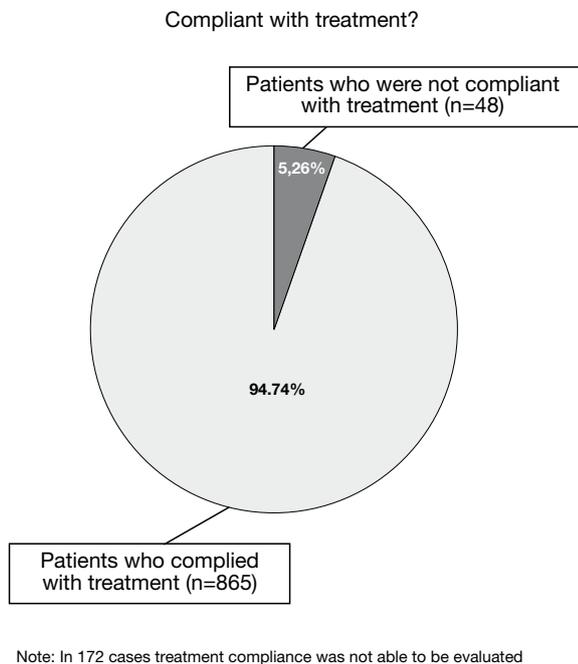


Figure 2. Oral lansoprazole treatment compliant patients. Note: In 172 cases it was impossible to calculate compliance to treatment.

Table 2

Percentage of oral lansoprazole treatment compliant patients in general and by patient groups

	N ^a	n ^b	% ^c	95% CI	p ^d
Total	913	865	94.74	93.29–96.19	
Men	393	370	94.15	91.83–96.47	.434
Women	512	488	95.31	93.48–97.14	
Between 18 and 35 years	69	64	92.75	86.64–98.87	
Between 35 and 54 years	333	317	95.2	92.9–97.49	
Between 55 and 74 years	429	409	95.34	93.34–97.33	.466
Over 75 years	70	64	91.43	84.87–97.99	
No concomitant disease	318	305	95.91	93.74–98.09	.199
With concomitant disease	572	537	93.88	91.92–95.85	
No concomitant treatment	247	238	96.36	94.02–98.69	.158
With concomitant treatment	630	592	93.97	92.11–95.83	
No difficulty in taking the drug	779	741	95.12	93.61–96.63	.162
Difficulty taking the drug	127	117	92.13	87.44–96.81	

Abbreviations: CI, confidence interval.

^a Number of patients with/without therapeutic compliance in which data was available.

^b Number of patients with therapeutic compliance.

^c Porcentaje calculado sobre n/N.

^d χ^2 test.

patients. Results show excellent compliance with treatment with the oral formulation of lansoprazole by the patients in the context of a common clinical practice of traumatology. In addition, oral lansoprazole treatment was well accepted by the patients.

The general rate of compliant patients was 94.74%, and over 90% in the different subgroups of patients according to gender, age, disease and concomitant treatment, perception of difficulty in taking pills and drug acceptance. The mean degree of general compliance was 94.5 (12.12). Patients with no concomitant disease or treatment and no difficulty taking pills complied significantly better.

Results obtained from the present study show that 79.69% of patients was "in complete agreement" or "in agreement" with the fact that oral lansoprazole helped them comply better with treatment. This supports previous results on the fact that patient preference for a determined form of administration seems related to

Table 3

Degree of compliance in oral lansoprazole treatment in general and by patient groups

	n ^a	Mean (SD)	p ^b
Total	913	94.50 (12.12)	
Men	393	94.38 (12.71)	.664
Women	512	94.66 (11.65)	
Between 18 and 35 years	69	93.37 (15.8)	.924
Between 35 and 54 years	333	94.35 (13.22)	
Between 55 and 74 years	429	94.97 (10.02)	
Older than 75 years	70	93.62 (14.5)	
Without concomitant disease	318	95.38 (11.9)	.003
With concomitant disease	572	93.96 (12.41)	
Without concomitant treatment	247	95.92 (10.40)	<.001
With concomitant treatment	630	93.89 (12.94)	
No difficulty in taking the drug	779	94.79 (11.8)	<.001
Difficulty in taking the drug	127	92.6 (14.05)	

Abbreviations: SD, standard deviation.

^a Patients in which data was available.

^b Mann-Whitney's U or Kruskal-Wallis test.

a larger adherence to drug therapy and, finally, with an increase in clinical improvement.¹⁴⁻¹⁷

Regarding acceptance, patients evaluated in a very positive way the different organoleptic characteristics of the drug, as well as the ease and comfort of taking the pills. These results confirm those from another unpublished study of the acceptance of oral lansoprazole, obtained by a primary care physician in the United Kingdom. This data, referred in the study by Baldi et al,² showed that between 83% (patients who took the drug without water) and 94% (patients who took the drug with water) considered the taste of the pill to be acceptable, between 91% (patients who took the drug without water) and 96% (patients who took the drug with water) had no problems taking the pills and 88% stated that they would request the new formulation from their physician. In our study, practically all of the patients positively evaluated the taste of the pills (96.41%) and stated that treatment was easy (91.35%) and comfortable (90.73%) to take, and in a similar way to what had been seen in the United Kingdom, most (94.81%) of the patients who had received previous treatment clearly preferred treatment with oral lansoprazole.

Both the results regarding compliance as well as those relative to acceptance observed in this study, with patients evaluated by traumatology, reproduce data published in the past by our team in patients treated in gastroenterology departments,²³ in which the drug was prescribed for treatment of gastric-esophageal reflux disease (GERD), and the patients were followed by primary care,²⁴ in which oral lansoprazole was prescribed as an acute treatment or for maintenance in GERD or as prevention for NSAID related gastric ulcers.

Finally, the function of the degree of acceptance of a drug over improvement in treatment compliance has been pointed out as a relevant aspect of previous studies.^{13,17,25} In the context of the traumatology consult, the use of lansoprazole, in most cases, is related to NSAID induced gastric pathology, supposing the patient does not notice the clinical improvement because he has no previous symptoms. Therefore, compliance is even more relevant and, in consequence, it is important to have alternate formulas to enable it. The results of this study show that oral lansoprazole have a comfortable formula which is clearly accepted by the patients, leading to an improved therapeutic compliance.

In the interpretation of the results of this study, we must take into account its intrinsic limitations. On one hand, the characteristics of study design and, on the other, the measurements and the population studied. With respect to design, the fact that it is not a comparative study does not make it possible to conclude that oral lansoprazole is superior to other formulations or treatments, limiting us to present only the patients subjective evaluation. In this sense, future research

Table 4

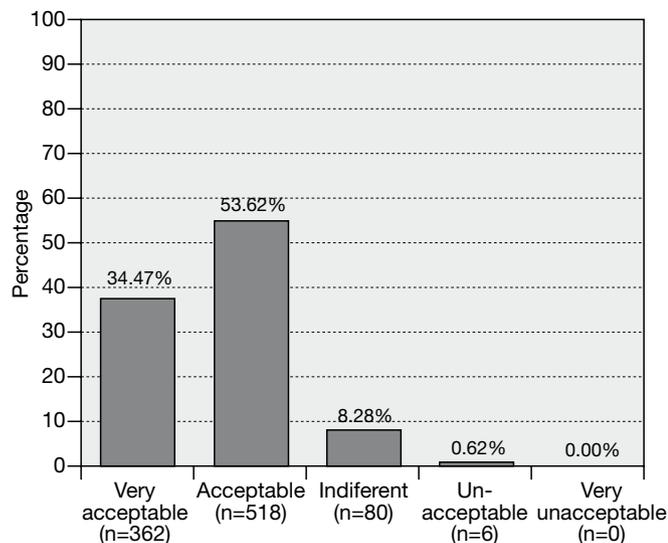
Evaluation of the organoleptic characteristics of oral lansoprazole

SIZE	Too big	Big	Neither big nor small	Small	Too small
n (%) ^a	4 (0.41)	149 (15.28)	628 (64.41)	194 (19.9)	0
TASTE	Very likable	likable	Neither likable nor disliked	Dislikable	Very dislikable
n (%) ^a	92 (9.45)	561 (57.6)	286 (29.36)	35 (3.59)	0
INTENSITY OF TASTE	Very mild	Mild	Neither strong nor mild	Strong	Very strong
n (%) ^a	7 (0.72)	143 (14.68)	473 (48.56)	327 (33.57)	24 (2.46)
SPEED OF DISSOLUTION	Very fast	Fast	Neither fast nor slow	Slow	Very slow
n (%) ^a	159 (16.29)	572 (58.61%)	175 (17.93%)	59 (7.07%)	1 (0.1)
ADEQUATE SPEED	Yes	No			
n (%) ^a	895 (91.7)	81 (8.3)			
AFTERTASTE	Yes	No			
n (%) ^a	452 (46.36%)	523 (53.64)			

^a Percentages calculated based on those patients in which data was available.**Table 5**

Evaluation of the properties of oral lansoprazole and perception of compliance

EASE OF USE	Very easy	Easy	Neither easy nor hard	Hard	Very hard
n (%) ^a	412 (42.43)	475 (48.92)	77 (7.93%)	7 (0.72)	0
COMFORT OF USE	Very comfortable	Comfortable	Indifferent	Uncomfortable	Very uncomfortable
n (%) ^a	424 (43.67)	457 (47.06)	82 (8.44)	8 (0.82)	0
SUBJECTIVE PERCEPTION OF COMPLIANCE	Completely in agreement	Agreement	Undecided	In disagreement	Completely in disagreement
n (%) ^b	284 (29.28)	489 (50.41)	167 (17.22)	30 (3.09)	0

^a Percentage calculated on total patients specifying the data (n=971).^b Percentage calculated on total patients specifying the data (n=970).**Figure 3.** Degree of acceptance of oral lansoprazole. Note: 119 patients had incomplete data.

should incorporate comparative treatments in order to confirm the positive results of this work.

In regard to the evaluation measurements, it must be pointed out that we did not employ a drug recount for compliance evaluation. On the other hand, although it has been seen that some patients tend to overestimate their compliance when asked directly,²² the use of interviews, as contemplated by the Haynes-Sackett²¹ test

employed in this study, correlates positively with the recount of capsules and seems to be the most useful quantitative measure, and the easiest one to use, when evaluating patient compliance. The application of the Haynes-Sackett test, added to the fact that acceptance was evaluated on strong elements, would support the validity of the conclusions obtained in the present study. Another limitation is not to have included special populations, especially persons with lifestyles which would limit access to liquid or particular problems with swallowing, in which a particular evaluation of acceptance and its possible influence on treatment compliance would be merited.

In conclusion, the present study shows an elevated degree of treatment compliance with oral lansoprazole, in addition to very good tolerance, acceptance and preference on the part of the patients. This data provides clinical elements for judgment based on a common clinical practice and under real drug use conditions, that may contribute to optimize a personalized therapeutic approach of patients treated by traumatology.

Conflict of interest

Authors E. Márquez, V. Gil, A. Nadal have received economic support for carrying out this study as members of the scientific committee. In addition, they confirm that within the study context there is no agreement by which they will benefit or receive payment on the part of any commercial entity. On the other hand, no commercial entity has paid or will pay foundations, educational commissions or other non-profit organizations to which they are affiliated.

Authors M.J. Plazas, J. Heras, and J. Porcel are medical advisors or are employed indirectly for Almirall Laboratories S.A., Barcelona.

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