

Letters to the Editor

Self-management of Vitamin K Antagonists Is More Cost-effective Than Dabigatran for Stroke Prevention in Non-valvular Atrial Fibrillation in Spain

El autocontrol de la terapia con cumarínicos es más eficiente que dabigatrán para prevenir ictus en fibrilación auricular no valvular en España

To the Editor,

We read with great interest the article by González-Juanatey et al.¹ on the cost-effectiveness of the new oral anticoagulant dabigatran compared with conventional oral anticoagulant therapy (OAT) in patients with nonvalvular atrial fibrillation. This study consisted of a simulation using modern computer models applied to the Spanish setting. It concluded that dabigatran would be an effective strategy for stroke prevention when compared with two different scenarios: 100% of patients on OAT, or the usual prescription pattern (60% on OAT, 30% on aspirin, and 10% untreated). The authors concluded that dabigatran is efficient because the increase in costs does not exceed 30 000 euros/quality-adjusted life year gained, an acceptability threshold proposed in 2002.¹ Increases in the cost-effectiveness ratio would be 17 581 euros/quality-adjusted life year for the scenario in which 100% of patients received OAT and would be 14 118 euros/quality-adjusted life year when the usual prescription pattern was considered. These results rely exclusively on data from the RE-LY (Randomized Evaluation of Long Term Anticoagulant Therapy) clinical trial, which compared dabigatran with OAT managed exclusively in specialist units on a monthly basis.² However, while González-Juanatey et al.'s¹ simulation takes into account the costs of different OAT management scenarios and includes weekly self-management, it does not consider the very different rate of serious complications observed depending on the model of OAT management used. For example, risk is clearly reduced by self-management compared with conventional OAT.³ Given the clinical and economic importance of these issues, clarification of some issues would seem opportune.

The design, procedure, and interpretation of the results of the RE-LY trial have attracted considerable criticism⁴; one of the major criticisms focused on the total lack of an advantage for dabigatran compared with conventional OAT when levels of international normalized ratio control, measured as the proportion of time in therapeutic range, are over 65% to 70%. It is unsurprising, therefore, that a recent publication⁵ which indirectly compared dabigatran and OAT self-management showed no significant difference in serious complications. On the contrary, there was a clear trend favoring self-management: the relative risk and its confidence intervals were 0.73 (0.48-1.10) for thromboembolism, 0.64 (0.40-1.01) for mortality, and 1.15 (0.83-1.60) for severe bleeding.⁵ Although direct comparative studies are lacking, these data should prompt health officials to rethink strategies for stroke prevention. Such a reevaluation is especially pertinent, given that 50% of patients receiving OAT in Spain can perform self-management with clinical guarantees⁶ and that a rigorous metaanalysis has confirmed the superiority of the self-management model over conventional OAT in specialized centers.³ Consequently, the last

international consensus of the American College of Chest Physicians recommended OAT self-management as the model of choice.⁷

Furthermore, the current cost of self-control in Spain is 420 euros/year, including technology, reagents, supervision, and data centralization,⁸ and not 884 euros to 1221 euros/year as erroneously stated in the article by Gonzalez-Juanatey et al.¹

Given the data presented, OAT self-management is clearly the most effective strategy for stroke prevention in patients with atrial fibrillation: its clinical outcomes are superior to those of conventional OAT and are not inferior to those of dabigatran. In addition, OAT self-management is highly cost-competitive compared with dabigatran (420 euros vs 1106 euros/year) and is competitive when compared with conventional control (420 euros vs 378-462 euros/year). The self-management model will therefore be the dominant pharmacoeconomic model (net savings) regardless of the type of analysis used.

CONFLICTS OF INTEREST

Juan Carlos Souto is the Scientific Director of Monitor Medical. He has received speaker's fees from Roche Diagnostics, Astra-Zeneca, and Sanofi-Aventis and reimbursement for attending conferences from Boehringer Ingelheim, Baxter, and Rovi. Xavier Ruyra is a consultant on valvular disease at Monitor Medical. Antoni Bayes-Genis has received reimbursement to attend meetings from Boehringer Ingelheim and Almirall and is a member of Monitor Medical's Scientific Advisory Board.

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Self-management of Vitamin K Antagonists Is More Cost-effective Than Dabigatran for Stroke Prevention in Non-valvular Atrial Fibrillation in Spain. Response

El autocontrol de la terapia con cumarínicos es más eficiente que dabigatrán para prevenir ictus en fibrilación auricular no valvular en España. Respuesta

To the Editor,

We feel that, in their letter, Souto et al. have not taken into account a series of highly relevant points concerning the results of our article and the topics raised.¹

First, the argument that treatment with vitamin K antagonists is more cost-effective is not supported by evidence, since there are no economic evaluations that compare the 2 options. In addition, the authors interpret the results cited of the indirect comparison of the efficacy of self-management vs dabigatran as a “clear trend favoring self-management”, whereas the original study found no statistically significant differences in any of the variables analyzed.

Second, in our study, the key factor indicating the advantage of dabigatran over warfarin in terms of the cost-effectiveness ratio was not the cost of monitoring the international normalized ratio, but the difference in the efficacy of the two agents, especially with respect to the risk of ischemic stroke (see Table 7 in Juanatey et al.¹).

Third, self-management of oral anticoagulation therapy is known to be very infrequent in the Spanish population (1%-2%).

Fourth, and highly relevant, as explained in our Table 3, our estimate of the cost of international normalized ratio monitoring was obtained by weighting the different modalities of oral anticoagulation therapy monitoring employed in Spain (primary care, in-hospital, home monitoring, self-monitoring) based on expert opinion and the best publicly-available evidence.²

To respond to the letter of Souto et al., we believe that the cost proposed by these authors, and the difference between the 2 sources still does not affect our results because self-management is performed by only 1% of all patients. To be precise, self-management would lead to a 1% cost reduction in monitoring in well controlled patients (382.2 euros vs 378.2 euros) and to a 2% reduction in poorly controlled patients (472.7 euros vs 464.7 euros). A related issue is that the authors fail to consider that our study included a sensitivity analysis of this variable, which examined the extent to which the incremental cost-effectiveness ratio differed if we varied the cost of international normalized ratio monitoring by $\pm 30\%$; this analysis showed that the costs obtained were also under euros 30 000/quality-adjusted life-year gained. Finally, the authors' estimate of 420 euros (private service fee for supervised self-management) does not take into account periodic visits to the physician, funded by the Spanish National Health System, whose perspective is the relevant issue in this analysis.

Given all of the above, we consider that the conclusion of Souto et al.—“The self-management model will therefore be the dominant pharmacoeconomic model (net savings) regardless of

the type of analysis used”—to only be a hypothesis. Thus, the aforementioned statement and the title of the letter should, at the very least, be expressed in the conditional tense.

CONFLICTS OF INTEREST

All of the authors of the original article have contributed to this response. Two of the authors (N. González-Rojas and V. Becerra) are employees of Boehringer Ingelheim. Another author (I. Oyagüez) is a member of Pharmacoeconomics & Outcomes Research (PORIB), a consultancy that specializes in financial analysis, which assisted Boehringer Ingelheim in an advisory capacity in relation to this study.

However, in no case did this situation influence the results presented.

José R. González-Juanatey,^a José M. Lobos,^b Joan C. Reverter,^c and Virginia Becerra,^{d,*} on behalf of all of the authors of the article $\diamond$

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$\diamond$ “Cost-effectiveness of Dabigatran for Stroke Prevention in Non-valvular Atrial Fibrillation in Spain” (José R. González-Juanatey, José Álvarez Sabin, José M. Lobos, Antoni Martínez-Rubio, Joan Carles Reverter, Itziar Oyagüez, Nuria González-Rojas, and Virginia Becerra).

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