

## Letters to the Editor

## Cost-effectiveness of Evolocumab



## Coste-efectividad del evolocumab

## To the Editor,

In recent decades, heart disease patient care has improved notably, largely due to constant treatment innovations. However, when it comes to evaluating the introduction of any new medication into clinical practice, it is important not only to determine the efficacy and safety of the particular drug, but also its incremental cost, as any therapeutic novelty usually involves a higher cost than the previous treatment, to capture the value of the innovation.

In this context, the cost-effectiveness study performed on evolocumab is of great interest.<sup>1</sup> The reader may recall that in the FOURIER study, with 27 564 patients with atherosclerotic cardiovascular disease and low-density lipoprotein cholesterol (LDL-C)  $\geq 70$  mg/dL despite statin treatment, the addition of evolocumab was associated with a significant reduction of 15% in the primary outcome variable (cardiovascular death, myocardial infarction, stroke, hospitalization due to unstable angina/coronary revascularization) and of 20% in the main secondary outcome (cardiovascular death, myocardial infarction or stroke), after 2.2 years of follow-up.<sup>2</sup> Of course, being a more expensive therapeutic option, it is important to have data on cost-effectiveness.

While we recognize the work carried out by the authors, we believe that some assumptions put into question the validity of the results and the conclusions.

First, the timeframe of the evaluation. In the study, 2 analyses were performed with 2 models with different timelines, at 26 months (decision tree model) and at 10 years (Markov model). We consider these timelines to be inappropriate since the study was about patients with chronic ischemic heart disease, with a longer mean survival. In addition, lipid-lowering therapy, especially the more intensive regime, affects survival, therefore a time horizon of a lifetime may be more appropriate.<sup>3</sup>

Regarding the costs incurred from each of the interventions, it is simply not possible to accept the calculations performed as valid. It appears that the annual cost of each intervention was applied to each monthly cycle, resulting in treatment costs markedly higher than expected. For example, if the estimated annual cost of evolocumab is €4969.74, how is it possible that the results from the Markov model (at 10 years) showed a cost of €471 714? Furthermore, according to the authors, the annual cost of treatment with statins is €104.87 (€8.70 per month). Given that the cost per 28 tablet-pack of atorvastatin 20, 40, and 80 mg is currently €9.21, €18.42, and €36.84, respectively, it appears that the cost has been underestimated. Similarly, analyzing the data published, we estimate that less than 12% of the patients would have been taking ezetimibe, a figure that seems too low bearing in mind the increasing use of combined lipid-lowering therapy. We also noted that the costs applied to the events appear to be lower than the published costs, which would penalize the more effective treatment.<sup>4</sup>

Another relevant aspect is that the cost-effectiveness analysis was done taking into account the total FOURIER population, whose inclusion required an LDL-C  $\geq 70$  mg/dL<sup>2</sup>, while the patient population funded in Spain<sup>5,6</sup> must have established cardiovascular disease with LDL-C  $> 100$  mg/dL with the maximum tolerated statin dose, so, unless an adjustment was made for the baseline LDL-C

values, the observed results would hardly be applicable to our setting. Furthermore, only the first cardiovascular event was considered, and not recurrences, which could penalize the more effective treatment.

Finally, the authors acknowledge that “due to the lack of a threshold for this type of outcome in economic evaluation, it is difficult to draw conclusions that can confirm that treatment with evolocumab is or is not cost-effective”, yet they conclude that “treatment with evolocumab is not cost-effective”.

In summary, we believe that the limitations call into question the conclusion of the study, and therefore, we believe that the above-described assumptions need to be corrected to reflect the efficacy of the intervention analyzed within the context of the Spanish national health system.

## CONFLICTS OF INTEREST

C. Escobar and V. Barrios have received fees from Amgen for scientific presentations.

Carlos Escobar<sup>a,\*</sup> and Vivencio Barrios<sup>b</sup>

<sup>a</sup>Servicio de Cardiología, Hospital La Paz, Madrid, Spain

<sup>b</sup>Servicio de Cardiología, Hospital Ramón y Cajal, Madrid, Spain

\* Corresponding author:

E-mail address: [escobar\\_cervantes\\_carlos@hotmail.com](mailto:escobar_cervantes_carlos@hotmail.com) (C. Escobar).

Available online 7 July 2018

## REFERENCES

1. Olry de Labry Lima A, Gimeno V, Sierra JF, et al. Cost-effectiveness and budget impact of treatment with evolocumab versus statins and ezetimibe for hypercholesterolemia in Spain. *Rev Esp Cardiol*. 2018;71:1027–1035.
2. Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med*. 2017;376:1713–1722.
3. Kristiansen IS, Gyrd-Hansen D. Cost-effectiveness analysis based on the number-needed-to-treat: common sense or non-sense? *Health Econ*. 2004;13:9–19.
4. Planellas L, Sorio F, Restovic G, P-062. Coste de eventos cardiovasculares en España: una revisión de literatura. XXXV Jornadas de la Asociación de Economía de la Salud (AES). Granada, 17 al 19 de junio de 2015.
5. Agencia Española de Medicamentos y Productos Sanitarios. Informe de posicionamiento terapéutico-Evolocumab/V1/03032016. Madrid: Ministerio de Sanidad, Servicios Sociales e Igualdad. Available at: <https://www.aemps.gob.es/medicamentosUsoHumano/informesPublicos/docs/IPT-evolocumab-repatha.pdf>. Accessed 20 Apr 2016.
6. Anguita Sánchez M, Castro Conde A, Cordero Fort A, et al. Challenges in oral lipid-lowering therapy: position document of the Spanish Society of Cardiology. *Rev Esp Cardiol*. 2016;69:1083–1087.

## SEE RELATED CONTENT:

<http://dx.doi.org/10.1016/j.rec.2018.05.003>

<http://dx.doi.org/10.1016/j.rec.2018.05.031>

<https://doi.org/10.1016/j.rec.2018.04.028>  
1885-5857/

© 2018 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.