Cost-effectiveness of Evolocumab in Patients With High Cardiovascular Risk in Spain

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ABSTRACT

Purpose: Our objective was to assess the cost-effectiveness of evolocumab in patients at high risk of cardiovascular (CV) events from the Spanish National Health System perspective.

Methods: A Markov model was used to assess the cost-effectiveness (incremental [Δ] cost per Δ quality-adjusted life-year [QALY]; or cost utility) of evolocumab plus standard of care (SoC; statins) versus SoC, assuming lifetime treatment. Cohorts with baseline LDL-C >100 mg/dL and familial hypercholesterolemia (FH) or CV event history (secondary prevention [SP]) were considered. Lifetime CV event rates were predicted either (1) using risk equations considering local risk factors (Spanish Familial Hypercholesterolemia Cohort Study) adjusted to reflect the increased risk of FH patients or (2) using CV event rates from local registries (Information System for the Development of Research in Primary Care) for SP patients. LDL-C relative reductions from evolocumab trials (Evolocumab 140 mg Q2W (bi-weekly) and 420 mg QM (monthly)) were converted into CV event reductions using rate ratios per millimole per liter (mmol/L; 38.67 mg/dL) from a meta-analysis of statin trials (Cholesterol Treatment Trialists' Collaboration).

Findings: Predicted 10-year/lifetime CV risks were 50%/95% (FH) and 62%/82% (SP) for SoC and 27%/83% (FH) and 44%/69% (SP) for evolocumab plus SoC. Predicted 10-year/lifetime major CV event risks were 42%/86% (FH) and 47%/67% (SP) for SoC and 21%/68% (FH) and 31%/52% (SP) for evolocumab plus SoC. Predicted per patient-year rates of non-fatal/fatal CV events were 2.2/0.8 (FH) and 1.1/0.6 (SP) for SoC and 1.2/0.6 (FH) and 0.7/0.5 (SP) for evolocumab plus SoC. Predicted CV event reductions per mmol/L were 17% (FH) and 15% (SP). Evolocumab treatment was associated with increased QALYs and costs compared with SoC (FH: Δcost, €65,369; ΔQALY, 2.12; incremental cost-effectiveness ratio [ICER], €30,893; SP: Δcost, €42,266; ΔQALY, 0.93; ICER, €45,340).

Implications: Evolocumab plus to SoC may provide a cost-effective option for LDL-C lowering in FH and SP patients in Spain. (*Clin Ther.* 2017;39:771–786)

Key words: cardiovascular disease, cost-effectiveness, evolocumab, hypercholesterolemia, LDL-C, PCSK9 inhibitors.

INTRODUCTION

Cardiovascular disease (CVD) is a leading public health problem.[1] During the past 30 years, there

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have been major advances in the clinical management of CVD. However, CVD remains the leading cause of death in Europe, and it is associated with a high burden in terms of quality of life (QoL) and costs, both because of acute episodes and chronic stages of ill health.[1,2]

The establishment of elevated LDL-C as a main risk factor for CV risk has led to the development of effective LDL-C–lowering therapies. Clinical trials proving the efficacy of these therapies provide a robust evidence base. Most notable is a meta-analysis of 27 interventional trials (174,149 individuals; median follow-up of 4.9 years) conducted by the Cholesterol Treatment Trialists' Collaboration (CTTC), which found that for every 1-mmol/L (38.67 mg/dL) reduction in LDL-C, the annual risk of any major CV event (MACE) was reduced by 21% to 28%, with a continued benefit observed even with low LDL-C levels (<2.0 millimole per liter (mmol/L)).[3–5] Although lowering LDL-C is effective, lowering LDL-C more may be even more effective, and it appears that the prediction as suggested by the CTTC equation is confirmed by the results from the most recent CV outcomes trial for ezetimibe,[6] a non-statin therapy. This, given the remaining burden of CVD, opens perspective for even more potent strategies to lower LDL-C levels.

One such strategy is the use of evolocumab (Repatha*), a subcutaneously injected proprotein convertase subtilisin kexin 9 (PCSK9) inhibitor, which has been recently approved by the European Medicines Agency as an adjunct treatment to diet and maximally tolerated statin therapy for adults with hypercholesterolemia who require additional lowering of LDL-C level.[7–9] In Phase III clinical trials, among patients with primary hypercholesterolemia, evolocumab was effective at reducing LDL-C levels, including when added to statin therapy, or when administered to statin intolerant (SI) patients, or when administered as monotherapy, and in patients with primary hypercholesterolemia who were receiving statin therapy with or without other lipid-lowering drugs. Albeit not powered to indicate differences in the incidence of CV events, existing data are suggestive of benefit but require confirmation in adequately powered outcome trials.[7,8]

*Trademark: Repatha® (Amgen, Thousand Oaks, California).

In Spain, evolocumab is reimbursed for use in patients not controlled with highest tolerated doses of statins and established CVD (ECVD) with LDL-C levels >100 mg/dL, patients with homozygous and heterozygous FH not controlled with highest tolerated doses of statins and with LDL-C levels >100 mg/dL, and any patient in the previous subgroups who are SI and have LDL-C levels >100 mg/dL.[10]

The objective of this modeling study was to assess the cost-effectiveness (incremental [Δ] cost per Δ quality-adjusted life-year [QALY]; also referred to as a cost-utility analysis) of add-on evolocumab therapy compared with current standard of care (SoC; statin therapy) in patients with high CV risk within hypercholesterolemia from the Spanish National Health System perspective.

PATIENTS AND METHODS

An economic model[11] was adapted to assess the cost-effectiveness of evolocumab therapy in the following two distinct adult population subgroups: (1) patients with FH with or without prior CVD event history receiving evolocumab in addition to SoC (ie, maximally tolerated dose [MTD] of statin therapy) were compared with patients receiving SoC alone and (2) patients with prior CVD event history (secondary prevention [SP]) receiving evolocumab in addition to SoC (ie, MTD of statin therapy) were compared with patients receiving SoC alone.

The model outcomes include predicted CV event rates, LYs, QALYs, and direct costs. Differences in model outcomes for evolocumab added to SoC versus SoC are reported. Incremental cost-effectiveness ratios (ICERs), defined as Δcost per ΔQALY, are presented for evolocumab added to SoC versus SoC.

Model Structure

Markov models are widely used and accepted by the scientific community to model the progression of chronic diseases.[12,13] A specific disease is depicted as a set of different health states, and movements between states over discrete time periods ("cycles") occur with a given probability ("transition probability"). Estimates of health outcomes and costs are attached to each state in the model. By running the model over a large number of cycles ("temporal horizon"), the long-term health outcomes and costs associated with the