COMPARISON OF NON-STATIN LIPID-LOWERING THERAPIES (LLT) BY THEIR ANNUAL COST PER EFFECTIVELY TREATED PATIENT WITH VERY HIGH CARDIOVASCULAR RISK IN SPAIN

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INTRODUCTION

- Cardiovascular disease (CVD) is the leading global cause of morbidity and mortality,[1] straining healthcare systems and economies.[2,3]
- The 2019 ESC/EAS guidelines and its 2025 update recommend low-density lipoprotein cholesterol (LDL-C) levels <55 mg/dL (1.4 mmol/L) and ≥50% reduction from baseline for secondary prevention in very high-risk patients with atherosclerotic CVD (ASCVD).[4,5]
- Non-statin therapies with proven CV benefit, taken alone or in combination, are recommended for patients who are unable to control LDL-C levels and reduce the risk of CV events despite maximally tolerated statin therapy. The choice should be based on the magnitude of additional LDL-C lowering needed.[5]
- In Spain, reimbursement for these new agents is restricted to patients with primary hypercholesterolemia or mixed dyslipidemia and/or CVD whose LDL-C levels remain >100 mg/dL (2.6 mmol/L) despite maximum tolerated statin therapy, or when statins are contraindicated or not tolerated.[6]
- Real-world data show that 18% to 27% of Spanish CVD patients meet these criteria,[7,9] yet only 1% to 3.4% receive proprotein convertase subtilisin/kexin type 9 inhibitors (PSCK9i).[10]

OBJECTIVE

- **To perform a comparative cost-effectiveness analysis of non-statin LLTs for patients categorized at very high risk of recurrent CV events in Spain, for achieving LDL-C therapeutic targets.**

METHOD

Study cohort

- A hypothetical cohort of 2,000 patients with prior major ASCVD event including MI and stroke was generated using a Monte Carlo simulation, based on Cosin-Sales et al.,[9] a **retrospective study in patients with ASCVD receiving standard LLT**, mainly statins (*Figure 1*). LDL-C levels were assumed to follow a log-normal distribution.
- **Aligned with the reimbursed threshold in Spain,**[6] only those patients with LDL-C levels >100 mg/dL were considered.

Studied treatments

- Evolocumab 140 mg every 2 weeks (Q2W)/420 mg once a month (QM); alirocumab 75 mg Q2W, 150 mg Q2W, and 300 mg QM; inclisiran 300 mg at baseline and 3 months (Q3M) followed by every 6 months (Q6M); and bempedoic acid 180 mg once a day (QD) alone or in fixed-dose combination (FDC) with ezetimibe 10 mg QD (*Table 1*).

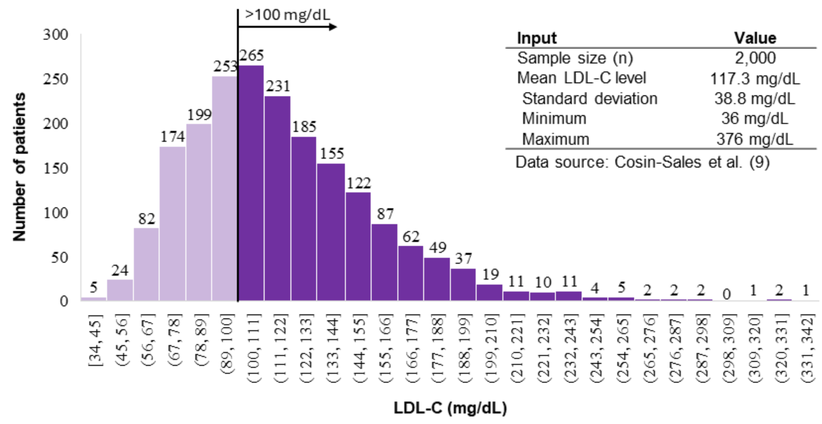
Effectiveness outcomes

- LDL-C lowering results were obtained from a **network meta-analysis of 48 randomized controlled trials of non-statin LLTs** added to maximally tolerated statins, including statin-intolerant patients (*Table 1*).[11]
- Based on these results, we simulated post-treatment LDL-C for each patient of the study cohort with each studied therapy and estimated the proportion of **effectively treated patients** (i.e., those achieving LDL-C <55 mg/dL and ≥50% LDL-C reduction from baseline, per 2019 & 2025 ESC/EAS guidelines).[4,5]

Costs and cost-effectiveness estimation

- Costs were estimated from the perspective of the Spanish National Health System and only considering the **direct pharmacological costs**.
- The **annual cost per effectively treated patient** was estimated in 4 different time scenarios (first year, second year, average of the first 2 and of the first 5 years) based on local annual treatment costs (2024 Euros, notified prices considering the 7.5% mandatory discount)[12,13] and treatment dosages (*Table 1*).
- The cost-effectiveness results are expressed as the cost per effectively treated patient and were calculated as equating to annual treatment cost / percentage of effectively treated patients.

Figure 1. Study cohort



Input	Value
Sample size (n)	2,000
Mean LDL-C level	117.3 mg/dL
Standard deviation	38.8 mg/dL
Minimum	36 mg/dL
Maximum	376 mg/dL

Data source: Cosin-Sales et al. (9)

Table 1. Model inputs

Studied treatment	Mean difference, % (95% CI)[a]	Annual treatment cost (€)[b]
Evolocumab 140 mg Q2W/420 mg QM	-65.44 (-68.37, -62.51)	4,956
Alirocumab 150 mg Q2W	-61.94 (-67.36, -56.51)	4,956
Alirocumab 75 mg Q2W	-53.17 (-56.61, -49.73)	4,956
Alirocumab 300 mg QM	-51.52 (-59.19, -43.85)	4,956
Inclisiran 300 mg Q3M to Q6M	-50.17 (-55.01, -45.34)	6,111 (Y1) 4,074 (Y2) 5,092 (avg Y1-2) 4,481 (avg Y1-5)
Bempedoic acid 180mg QD/ezetimibe 10mg QD FDC	-37.90 (-46.69, -29.11)	943
Bempedoic acid 180mg QD	-18.38 (-23.78, -12.97)	943

[a]Mean difference in percentage change in LDL-C from baseline in response to LLT relative to placebo at week 12 in patients receiving statin background therapy (moderate-high intensity)[11]
[b]Based on local annual treatment costs (2024 Euros, notified prices considering the 7.5% mandatory discount)[12,13] and treatment dosages
CI, confidence interval; FDC, fixed-dose combination; LDL-C, low-density lipoprotein cholesterol; Q2W, every 2 weeks; Q3M, every 3 months; Q6M, every 6 months; QD, once a day; QM, once a month.

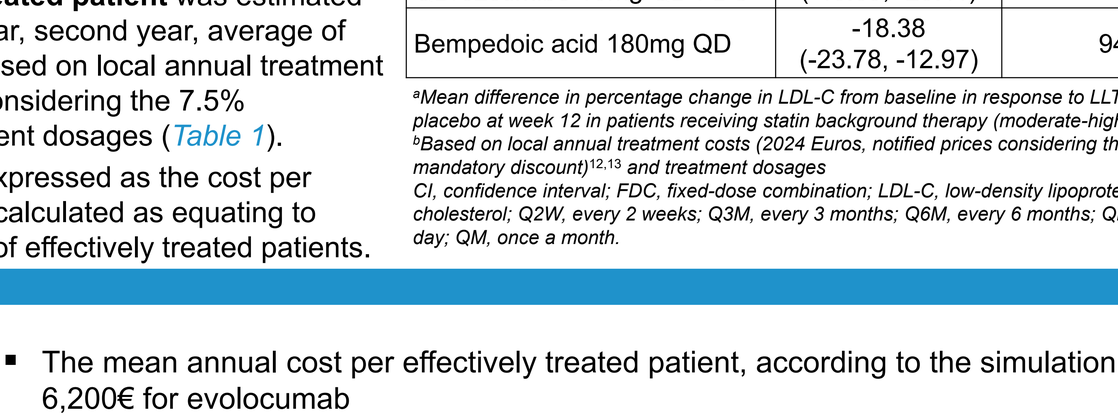
RESULTS

- Evolocumab 140 mg Q2W, followed by alirocumab 150 mg Q2W were modelled as the most cost-effective non statin LLTs, with 80% and 70% of patients treated effectively (i.e., achieving guidelines criteria), respectively (*Figure 2*).
- Modelled results for alirocumab 75 mg Q2W, alirocumab 300 mg monthly doses, and inclisiran were limited in magnitude, with only 33%, 26%, and 20% of patients treated effectively, respectively (*Figure 2*).
- The estimated rates for bempedoic acid 180 mg QD, alone or in combination, were 0% (*Figure 2*).

Figure 2. Proportion of effectively treated patients

- The mean annual cost per effectively treated patient, according to the simulation, was 6,200€ for evolocumab 140 mg Q2W, 7,127€ for alirocumab 150 mg Q2W (+15% vs evolocumab), 15,159€ for alirocumab 75 mg Q2W (+144% vs evolocumab), and 19,255€ for alirocumab 300 mg QM (+211% vs evolocumab) (*Figure 3*).
- Regarding inclisiran 300 mg Q3M to Q6M, its intensive initial posology and lower associated effectiveness rate resulted in higher costs per effectively treated patient in Year 1 (31,329€ [+405% vs evolocumab]) compared with the subsequent time scenarios (26,108€ [+321% vs evolocumab] and 22,975€ [271% vs evolocumab] over the first 2 and 5 years, respectively) (*Figure 3*).

Figure 3. Annual cost per effectively treated patient



[a] In case the lower bound of the CI for the effectiveness outcome was 0, the calculus of the respective cost effectiveness ratio was non-estimable.
[b] Compared to annual cost per effectively treated patient with evolocumab 140 mg Q2W.

CONCLUSIONS

- **Adding evolocumab 140 mg Q2W to background statins, compared to other LLTs used in the secondary prevention setting, resulted in the highest proportion (80%) of very high-risk patients (with baseline LDL-C >100mg/dL) achieving the 2019 ESC/EAS LDL-C guidelines targets in our simulation.**
- **Evolocumab 140 mg was associated with the lowest mean annual cost per patient effectively treated (6,200€) vs other LLT treatments.**

REFERENCES

1. World Health Organization - The top 10 causes of death. Available at: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death. **2.** Mensah GA, et al. *J Am Coll Cardiol.* 2023;82(25):2350–473. **3.** Luengo-Fernandez R, et al. *Eur Heart J.* 2023;44(45):4752–67. **4.** Mach F, et al. *Eur Heart J.* 2020;41(1):111–88. **5.** Mach F, et al. *Eur Heart J.* 2025;ehaf190. **6.** BIFIMED - Nomenclátor de NOVIEMBRE - 2024. Available at: https://www.sanidad.gob.es/profesionales/medicamentos.do. **7.** Zamora A, et al. *Rev Esp Cardiol.* 2018;71(12):1010–7. **8.** Cordero A, et al. *Rev Esp Cardiol.* 2019;72(6):518–9. **9.** Cosin-Sales J, et al. *Adv Ther.* 2023;40(6):2710–24. **10.** Zamora A, et al. *Rev Esp Cardiol.* 2019;72(6):519–20. **11.** Toth PP, et al. *J Am Heart Assoc.* 2022;11(18):e02555. **12.** Bot Plus. Available from: https://botplusweb.farmaceuticos.com/. **13.** Real Decreto-ley 8/2010. Available from: https://www.boe.es/buscar/act.php?id=BOE-A-2010-8228.

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