7019

A COST PER RESPONDER ANALYSIS OF LIPID-LOWERING THERAPIES IN PATIENTS WITH ESTABLISHED ATHEROSCLEROTIC CARDIOVASCULAR DISEASE IN ITALY

ABSTRACT ID 7019 EE8

P.A. CORTESI[1,2], D. MARCHESINI[3], V. MANFREDA[4], S. SAMMAK[4], I. C. ANTONAZZO[1,2], L.G. MANTOVANI[1,2]

1. Research Centre on Public Health (CESP), University of Milano-Bicocca, MB, Italy
2. Laboratory of Public Health, IRCCS Istituto Auxologico Italiano, Milan, Italy
3. Fondazione Charta, Milan, Italy
4. Value & Access Department, Amgen Srl, Milan, Italy

INTRODUCTION

- Hyperlipidemias represent one of the most important causal factors of early manifestations of atherosclerosis and organ damage, such as acute myocardial infarction (AMI), cerebral stroke and peripheral vascular disease.[1]
- Low-density lipoprotein cholesterol (LDL-C) is a main target of hypolipidemic treatments in primary and secondary prevention.[2]
- New effective drugs have shown a significant reduction of LDL-C level; however, a systematic assessment of their value in reaching LDL-C target level indicated by international guidelines is lacking.

OBJECTIVE

- **Assessing the value of lipid lowering therapies (LLTs) in reaching LDL-C targets recommended by 2019 EAS/ESC guidelines,[3] through a cost per responder analysis in patients with atherosclerotic cardiovascular disease (ASCVD) and uncontrolled hypercholesterolemia after statin therapy (an eligibility criterion for LLT per the Italian National Health system).**

METHOD

Methodological Steps	Purpose and Source Data Selected
1. Microsimulation analysis	• Estimate and compare the cost per responder associated to the treatments with LLTs used in Italian clinical practice: - Bempedoic acid ± ezetimibe - Inclisiran - Alirocumab - Evolocumab
2. Mean LDL-C in the simulated population	• Mean value ± standard deviation [SD] : 147.6 [± 35.2] mg/dL[4]
3. Cost analysis	• The analysis used a one-year time horizon • It included the cost related to the drug acquisition and the efficacy data associated to the each LLTs in reaching the 2019 EAS/ESC guidelines LDL-C targets < 40 mg/dL and < 55 mg/dL.[3]
4. Drugs' ex-factory price	• The drugs' ex-factory price net of statutory discounts were retrieved from the Italian Medicines Agency database at July 2025.[5]
5. Efficacy data of LLTs	• Efficacy data was obtained from a network meta-analysis of LLTs randomized trials.[6]
6. Main outcomes explored in the cost analysis	1. **Treatment cost (€) per patient reaching LDL-C targets < 40 mg/dL and** 2. **Treatment cost (€) per patient reaching LDL-C targets < 55 mg/dL** 3. **A scenario analysis was conducted to test a different baseline LDL-C level (128.3 ± 39.6 mg/dL) reported by the target population in another Italian real-world study.[7]**

RESULTS

- In the base case analysis, the highest percentage of responders was reported for evolocumab, as mean (95% confidence interval [CI]) (*Figure 1*):
  - At LDL-C target < 40 mg/dL: 25% [17% - 33%]
  - At LDL-C target < 55 mg/dL: 65% [53% - 76%]
- It was followed by alirocumab (16% [7% - 30%] and 51% [33% - 72%]), inclisiran (2% [0% - 5%] and 20% [13% - 29%]), and bempedoic acid ± ezetimibe (0% [0% - 1%] and 5% [1% - 15%]), (*Figure 1A and 1B, respectively*).
- The annual treatment cost per responder was the lowest (mean [95% CI]) for evolocumab (20,618€ [15,261€ - 29,284€] and 7,832€ [6,717€ - 9,540€]), followed by alirocumab (31,037€ [17,243€ - 74,719€] and 9,997€ [7,049€ - 15,237€]), and inclisiran (278,958€ [109,282€ - 1,325,049€] and (26.769€ [18,151€ - 42,233€]), at LDL-C < 40 mg/dL and < 55 mg/dL, respectively (*Table 1*).
- In the scenario analysis, using a lower baseline LDL-C level (128.3 ± 39.6 mg/dL) for the target population, all treatments reported a lower cost per responder compared to the base case (*Table 2*). Also in this scenario analysis evolocumab reported the highest value with the lowest cost per responder using LDL-C < 1.0 mmol/L (40 mg/dL) and a lower cost per responder, similar to bempedoic acid + ezetimibe, using LDL-C < 1.4 mmol/L (55 mg/dL).

Figure 1. Percentage of responder based on 2019 EAS/ESC guidelines

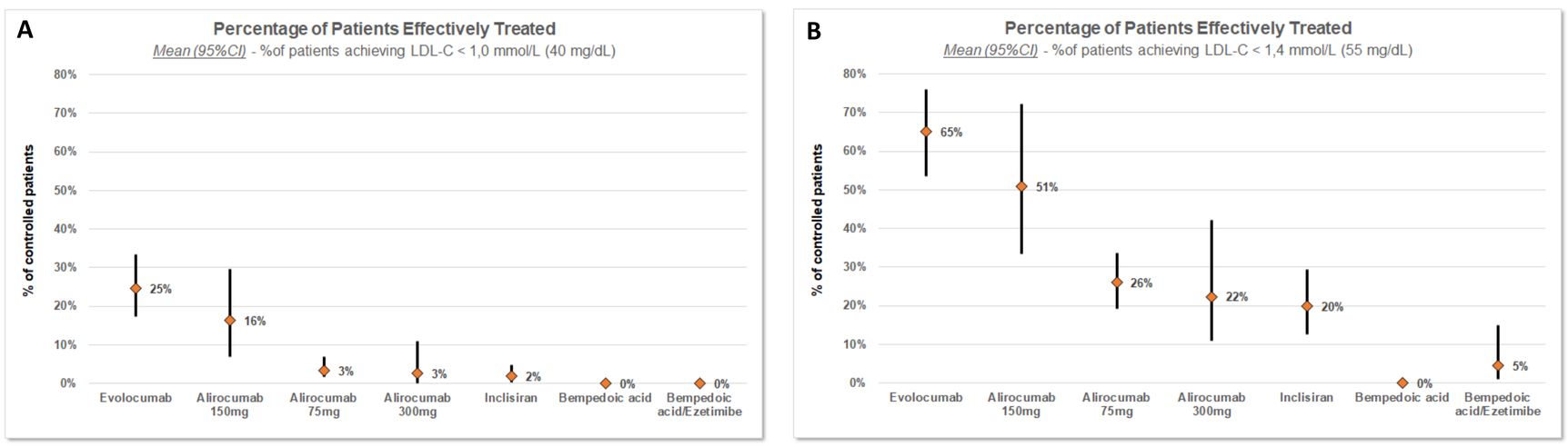

Table 1. Cost (€) per responder based on 2019 EAS/ESC guidelines

LLTs	Cost (€) per responder (LDL-C < 1.0 mmol/L (40 mg/dL),) Mean (95% CI)	Cost (€) per responder (LDL-C < 1.4 mmol/L (55 mg/dL)) Mean (95% CI)
Evolocumab	20,618 (15,261 - 29,284)	7,832 (6,717 - 9,540)
Alirocumab 150 mg	31,037 (17,243 - 74,719)	9,997 (7,049 - 15,237)
Alirocumab 75 mg	150,553 (73,095 - 296,678)	19,549 (15,078 - 26,475)
Alirocumab 300 mg	197,790 (46,485 - 10,087,296)	22,719 (12,095 - 46,700)
Inclisiran 284 mg	278,958 (109,282 - 1,325,049)	26.769 (18,151 - 42,233)
Bempedoic acid 180 mg	NA (NA - NA)	NA (NA - 375,996)
Bempedoic acid 180 mg + ezetimibe 10 mg	NA (NA - 144,614)	20,435 (6,373 - 85,454)

Table 2. Alternative scenario - Cost (€) per responder based on 2019 EAS/ESC guidelines

LLTs	Cost (€) per responder (LDL-C < 1.0 mmol/L (40 mg/dL)) Mean (95% CI)	Cost (€) per responder (LDL-C < 1.4 mmol/L (55 mg/dL)) Mean (95% CI)
Evolocumab	9,572 (7,775 - 11,947)	5,852 (5,525 - 6,261)
Alirocumab 150 mg	12,544 (8,279 - 22,822)	6,369 (5,611 - 7,763)
Alirocumab 75 mg	35,875 (22,443 - 63,140)	9,098 (7,731 - 11,235)
Alirocumab 300 mg	48,322 (16,358 - 591,948)	10,162 (6,964 - 16,414)
Inclisiran 284 mg	63,801 (28,933 - 242,754)	11,533 (8,700 - 15,195)
Bempedoic acid 180 mg	NA (NA - NA)	NA (NA - 53,489)
Bempedoic acid 180 mg + ezetimibe 10 mg	NA (NA - 25,582)	5,192 (2,479 - 15,349)

LLTs: lipid lowering therapies; CI, confidence interval

CONCLUSIONS

- **Among LLTs available in Italy, evolocumab reported the highest probability of reaching both 2019 EAS/ESC guidelines LDL-C targets <40 mg/dL and <55 mg/dL.**
- **Evolocumab reported also the lower cost for effectively treated patient resulting in the LLT with the highest value for treating ASCVD patient in Italy.**
- **This analysis can help decision makers identify the most cost-effective treatment to reach the desired clinical outcome and guiding the indication and funding of the use of LLTs in ASCVD patients in the Italian setting.**
- **Further studies are required to confirm these results on medium- and long-term time horizon and to assess the overall economic and health impact including the costs and clinical consequence of cardiovascular events experienced by these patients over time.**

REFERENCES

1. Mhaimeed O, et al. *Am J Prev Cardiol.* 2024;18:100649.
2. Fulcher J, et al. *Lancet* 2015;385:1397-405.
3. Mach F, et al., *European Heart Journal 2020;*41(1):111-188.
4. Gargiulo P,et al. *Atherosclerosis* 2023;366:32-39.
5. AIFA Lists of Class A and Class H medicinal products; available from: https://www.aifa.gov.it/en/liste-farmaci-a-h
6. Toth PP, et al. *J Am Heart Assoc.* 2022;11(18):e025551.
7. Presta V, et al. *Atherosclerosis* 2019;285:40-48.

ACKNOWLEDGEMENTS & FUNDING DECLARATIONS

- The study was supported by Amgen Inc.
- Fondazione Charta received funding from Amgen Srl to prepare the abstract and poster.
- Author disclosures:
  PAC: grants and personal fees from Novartis, Daiichi, Otsuka, Bayer, Almirall and Roche; **DM:** Fondazione Charta employee; **VM, SS:** Amgen employees and stockholders; **ICA:** no conflicts of interest; **LGM:** grants and personal fees from Bayer AG, Boehringer Ingelheim, Pfizer and Daiichi-Sankyo.

CONTACT

Davide Marchesini, PharmD
email: davide.marchesini@fondazionecharta.org