ECONOMIC EVALUATION OF CEFIDEROCOL FOR THE TREATMENT OF CONFIRMED MBL-PRODUCING PATHOGENS IN ITALY

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INTRODUCTION

- The spread of metallo-β-Lactamase (MBL)-producing Gram-negative pathogens is a major global health concern. MBL infections are linked to longer hospital stays, intensive care unit admissions, and higher mortality. Few therapeutic options effectively overcome MBL-mediated resistance.[1]
- Cefiderocol, a siderophore-cephalosporin indicated for the treatment of infections due to aerobic Gram-negative organisms with limited treatment options, has been recognized by AIFA (Italian Medicines Agency) as 'innovative' medicine for its *important added therapeutic value*.[2] Cefiderocol was launched in Italy in 2021.

OBJECTIVE

To assess the **cost-effectiveness** of cefiderocol versus colistin-based regimens for severe MBL-producing Gram-negative infections in the **Italian healthcare setting**, using a decision-tree-analytic model to estimate, over a 5-year horizon, the **Incremental Cost-Effectiveness Ratio (ICER)** per Quality-Adjusted Life Year (QALY) and the incremental **Net Monetary Benefit (NMB)**.

METHODS

TARGET POPULATION: patients with confirmed carbapenem-resistant (CR) infections caused by MBL-producing pathogens. A weighted average of three infection sites - complicated urinary tract infection (cUTI), pneumonia, and bloodstream infection (BSI/sepsis) - was included in the model. The distribution among infection sites was informed by prevalence data from Italy.[3]

MODEL DESIGN: initial decision node captured the rate of all-cause mortality at day 28 (ACM). Microbiological test results are assumed to be available at treatment initiation; therefore, pathogen strain and its antimicrobial susceptibility profile are known at the time patients enter the model.

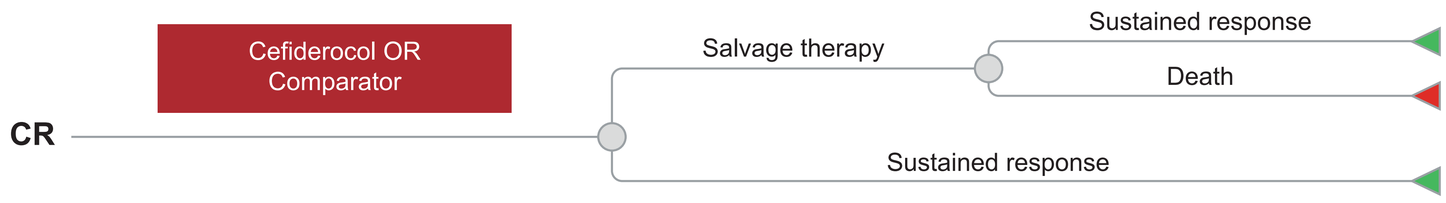


Figure 1: Summary of model structure

- **Clinical effectiveness**: The model used **day-28 ACM** from published patient-level data on MBL-producing bacterial infections from two phase 3, randomized, prospective, clinical studies investigating the efficacy and safety of cefiderocol (CREDIBLE-CR and APKENS-NP).[4] Overall ACM was 12.5% with cefiderocol and 50.0% with other agents.
- **Adverse events (AE)**: renal impairment and *Clostridium difficile* infection; therapy-related AE: ≥3% of patients.
- **Treatment costs**: EXF price in Official Gazette (cefiderocol); max selling price to NHS of class C products (colistin and treatments in combination with colistin).
- **Economic analysis**: Italian NHS perspective; 5-year horizon; 3% annual discounting of costs and QALYs.[5,6]
- **Cost-effectiveness threshold**: € 40,000 per QALY gained.[5]
- **Uncertainty analysis**: one-way deterministic and probabilistic (2,000 simulations).

RESULTS

Over 5 years, cefiderocol:

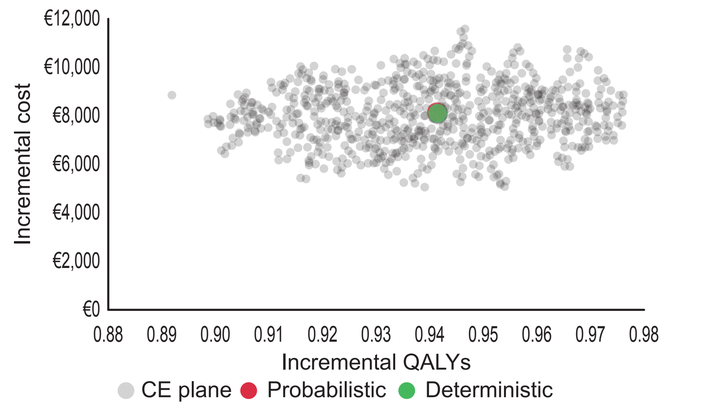
- gained **+0.941 QALYs** at an incremental cost of **€ 8,094** per patient.
- yielded an **ICER of € 8,599/QALY**.
- generated a positive **NMB** (**€ 29,556** at a € 40,000/QALY threshold).

Table 1. 5-year base-case cost-effectiveness analysis

	Cefiderocol	Comparator	Difference
Total cost	€ 20,475	€ 12,381	€ 8,094
QALYs	2.823	1.881	0.941
ICER			**€ 8,599**
NMB			**€ 29,556**

The mean incremental cost of the probabilistic sensitivity analysis is comparable to that of the base-case analysis. The probabilistic analysis confirmed **cost-effectiveness in 100% of 2,000 simulations** at the € 40,000 / QALY willingness-to-pay threshold.

Figure 2. Probabilistic analysis



Cost-effectiveness plane reporting the 2000 simulations of the probabilistic sensitivity analysis

The outcome measure used in the model (28-day ACM) is associated with some limitations, such as the low number of patients and the differences in study designs, comparator agents, and inclusion and exclusion criteria among the two studies.

CONCLUSIONS

Cefiderocol is a cost-effective intervention for treating carbapenem-resistant infections caused by MBL when compared with colistin-based regimens at the €40,000/QALY threshold.
Probabilistic simulations confirmed the **robustness of the model at 100%.**
Further research is warranted for comparisons to other antibiotics.

This analysis demonstrates the **cost-effectiveness of cefiderocol** in the treatment of critically ill patients with infection caused by **CR MBL-producing pathogens**

This finding is particularly relevant for clinical practice given the high unmet need and high mortality rates in patients with infections caused by MBL.

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DISCLOSURE

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Conflict of interest: MLN and DA are employees of Shionogi BV.