ECONOMIC EVALUATION OF CEFIDEROCOL FOR THE TREATMENT OF CARBAPENEM-RESISTANT *ACINETOBACTER BAUMANNII* IN ITALY USING REAL-WORLD EVIDENCE

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INTRODUCTION

- Antibiotic-resistance to carbapenems is a global top-priority concern. Infections caused by the Carbapenem-Resistant *Acinetobacter Baumannii* (CRAB) pose a major health risk, often resulting in fatal outcomes.
- Cefiderocol is a siderophore-cephalosporin indicated for the treatment of infections due to aerobic Gram-negative organisms in adults, with limited treatment options. It was launched in Italy in 2021.
- AIFA (Italian Medicines Agency) recognized cefiderocol as 'innovative' for its important *added therapeutic value*.[1]
  Given the unmet need and emerging comparative real-world evidence, this analysis was performed to assess the value of cefiderocol in this setting.

OBJECTIVE

To assess the **cost-effectiveness** of cefiderocol versus colistin-based regimens for severe CRAB Gram-negative infections in the **Italian healthcare setting**, using a decision-tree 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 CRAB severe infections. The distribution among infection sites was informed by prevalence data from Italy.[2]

MODEL DESIGN: the initial decision node captured rate of all-cause mortality (ACM) at day 28. 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.

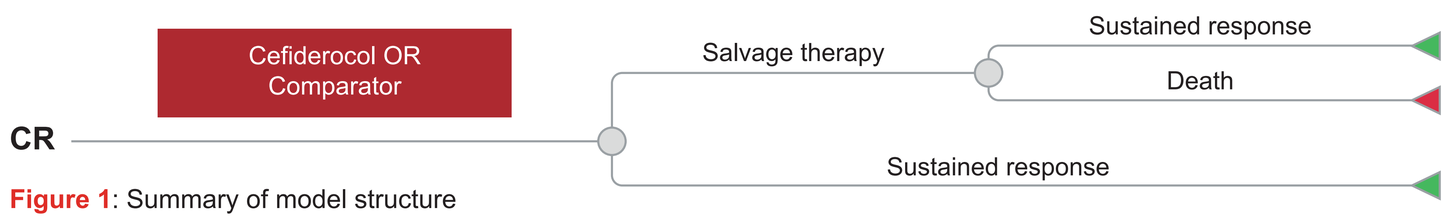


Figure 1: Summary of model structure

- **Clinical effectiveness**: The probability of **28-day ACM** for cefiderocol and colistin-based regimens (**OR = 0.53**; 95% CI 0.41–0.68; p < 0.0001) was obtained from a recent meta-analysis that pooled adjusted ORs from the studies identified by a SLR (1 RCT and 6 observational studies).[3]
- **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.[4,5]
- **Cost-effectiveness threshold**: € 40,000 per QALY gained.[6]
- **Uncertainty analysis**: one-way deterministic and probabilistic (2,000 simulations).

Table 1. Treatment-specific costs

	Unit cost	Units per pack	Units required per day	Daily cost
Cefiderocol	€ 1,500	10	6	€ 900
Colistin[a]	€ 280	10	9	€ 252

[a] Average price per MIU, dose of 9MIU per day

Table 2. Hospital costs stratified by ward

	Cost per day	
	Pneumonia	BSI and Sepsis
General ward*	€ 255	€ 404
Ventilation#	€ 309	€ 932
Intensive care unit[7]	€ 1,383	€ 1,383
Lenght of hospital stay§	10.3 days	18.2 days

*Average cost per SDO 2021 LOS for each DRG 090, 576
#Average cost per SDO 2021 LOS for each DRG 089; 575
§Average LOS reported by SDO 2021

RESULTS

Over 5 years, cefiderocol:

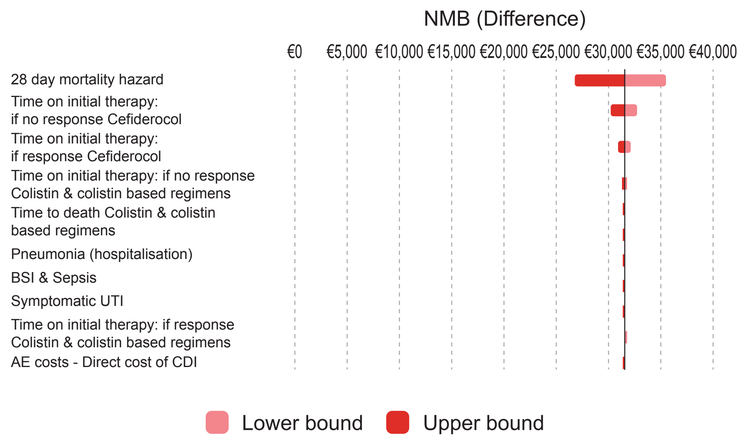
- gained **+0.929 QALYs** at an incremental cost of **€ 8,243** per patient
- yielded an **ICER of € 8,871/QALY**
- generated a positive **NMB** (**€ 28,923** at a € 40,000/QALY threshold)

Table 3. **5-year base-case cost-effectiveness analysis**

	Cefiderocol	Comparator	Difference
Total cost	€ 20,652	€ 12,410	€ 8,243
QALYs	2.337	1.408	0.929
ICER			**€ 8,871**
NMB			**€ 28,923**

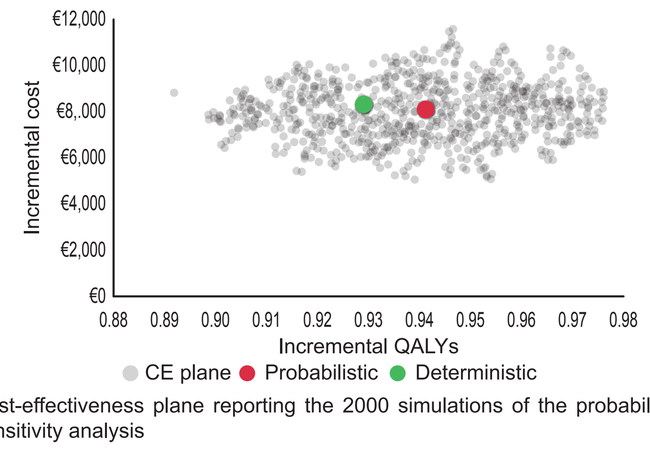
In terms of NBM, the **28-day mortality hazard ratio** of cefiderocol versus colistin-based regimens is the **primary driver of cost-effectiveness**.

Figure 2. **Net Monetary Benefit outcome**



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 3. **Cost-effectiveness Plane**



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

Limitations: 1) assumed availability of microbiological results and accurate knowledge of the sensitivity profile at the beginning of treatment, conditions not always found in clinical practice; 2) in the meta-analysis, the number of included studies was limited, although only studies providing adjustments for confounders among patients treated with cefiderocol-based or colistin-based regimens were included.

CONCLUSIONS

Despite the aforementioned limitations, the results of the analysis conducted in the light of the **new comparative real-world evidence representative of the Italian healthcare context**, confirm that cefiderocol represents a cost-effective strategy for the treatment of CRAB infections in Italy. This finding is particularly relevant for clinical practice in a setting characterized by a significant impact of resistant infections on mortality and healthcare resources and by **limited therapeutic options**.

Based on Italian RWE, **cefiderocol is a cost-effective intervention for treating carbapenem-resistant infections caused by CRAB when compared with colistin-based regimens** at the €40,000/QALY threshold

Probabilistic simulations confirmed the **robustness of the model at 100%.**

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DISCLOSURE

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