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Quantifying the value of aztreonam-avibactam in treating suspected metallo-β-lactamase producing Enterobacterales infections in Greece: A STEDI value approach

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The aim of the study was to quantify the value of aztreonam-avibactam (ATM- AVI) considering value elements from the **STEDI** antimicrobial value framework

Considering **T**ransmission and **D**iversity value the ATM-AVI provides

€1.54 billion

of value over 10 years to the Greek healthcare system

Introducing ATM-AVI was associated with reduced costs and quality-adjusted life year (QALY) gains, driven by fewer deaths

Conclusions

- The addition of ATM-AVI to the Greek healthcare system is dominant and urgently needed
- There is an urgent unmet need for new antimicrobials, but they are not an attractive investment
- Currently the full value to healthcare systems is not assessed in economic evaluations and health technology assessment of antimicrobials
- To support policy advancements future models should consider the remaining elements of the STEDI framework to quantify the full benefits of antimicrobials

Introduction

- Greece faces the highest epidemiological burden among European countries, with high incidence of infections caused by multi-drug resistant (MDR) pathogens and high rates of mortality[1]
- Metallo-β-lactamase producing Enterobacterales (MBL-PE) comprise a significant subpopulation of MDR pathogens with mortality rates up to 36% due to a lack of active effective treatments.[2] This underpins the urgent and serious unmet medical need for new antibiotics targeting MBL-PE
- Aztreonam-avibactam (ATM-AVI) is approved in Europe in adult patients for the treatment of complicated intra-abdominal infection (cIAI); hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP); complicated urinary tract infection, including pyelonephritis and for infections due to aerobic gram-negative organisms with limited treatment options (LTO)
- Quantifying the broader value of antimicrobials, considering the spectrum, transmission, enablement, diversity, and insurance (STEDI) framework, is crucial to appropriately value antimicrobials and reinvigorate the clinical pipeline

Objective

This study assessed the value and cost-effectiveness of ATM-AVI for the treatment of hospital-acquired infections caused by suspected MBL-PE in Greece, considering the transmission and diversity value of the STEDI framework

Methods

Design: A dynamic transmission model was developed to quantify the value of adding ATM-AVI into the treatment strategy cIAI and HAP/VAP, confirmed or suspected to be caused by MBL-PE, in Greece. Aligned to the phase 3 REVISIT trial population

- The model considers the impact of introducing ATM-AVI on the ability to effectively treat infections and on the population-level resistance, over a 10-year horizon from a Greek payer perspective

Treatments: ATM-AVI was assessed as an additional intervention, positioned first-line, to the current two-line treatment strategy:

Comparator	Colistin + meropenem	〉	Colistin + aminoglycoside	
Intervention	ATM/AVI	〉	Colistin + meropenem	〉 Colistin + aminoglycoside

Clinical inputs: the model was populated with clinical data from the phase 3 REVISIT trial from the perspective of the Greek healthcare payer. Prevalence of MBL-PE HAIs and resistance was sourced from the literature[3,4]

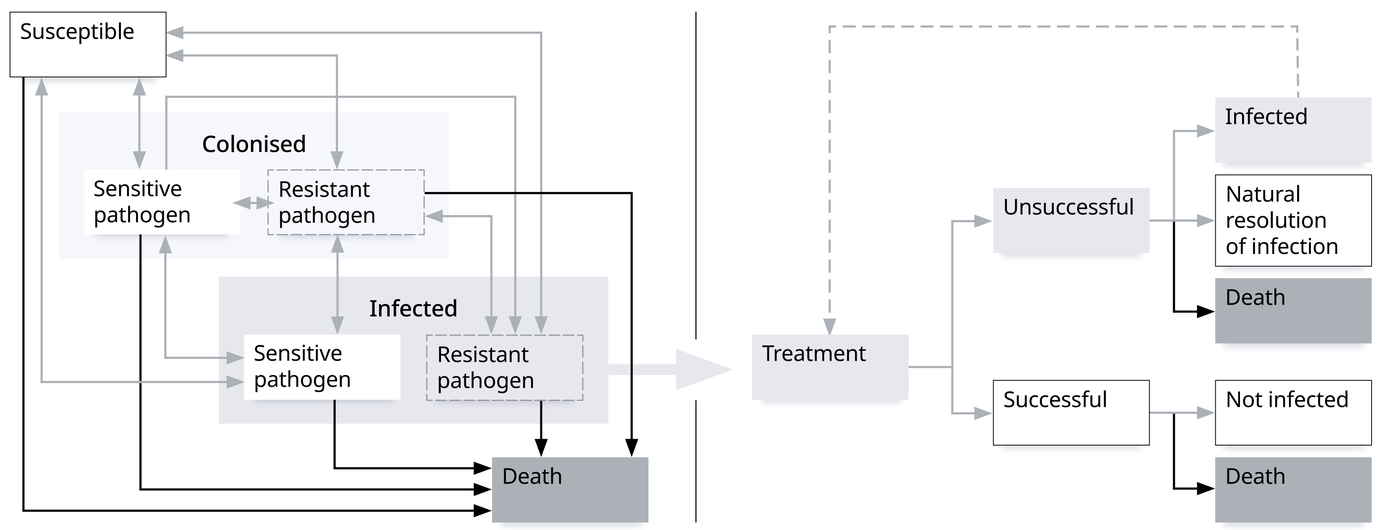
Adverse events: the model included treatment-related adverse events (TRAE) for nephrotoxicity and *Clostridium difficile*, as two of the most clinically significant TRAE associated with the modelled treatments

Costs: antimicrobial acquisition costs were taken from the Official Price Bulletin,[5] and hospitalisation costs were taken from the Greek Diagnosis Related Groups published in Government Gazette.[6] Costs were included for the treatment of adverse events

Resource use: the model assumed a hospital length of stay (LOS) for the duration of treatment (cIAI: 7.5 days; HAP/VAP: 10.5 days)[7] and 3 days for unsuccessful treatment before changing treatment. An additional 7 days LOS was assumed for patients who die

Model design

Figure 1. Model schematic of dynamic transmission model and treatment decision tree



Results

The model estimated over **10 years**, 13,082 and 11,361 patients were treated for cIAI and HAP/VAP caused by MBL-PE, in Greece, under the current treatment strategy and with the addition of ATM-AVI, respectively

The introduction of ATM-AVI as a first-line treatment resulted in:

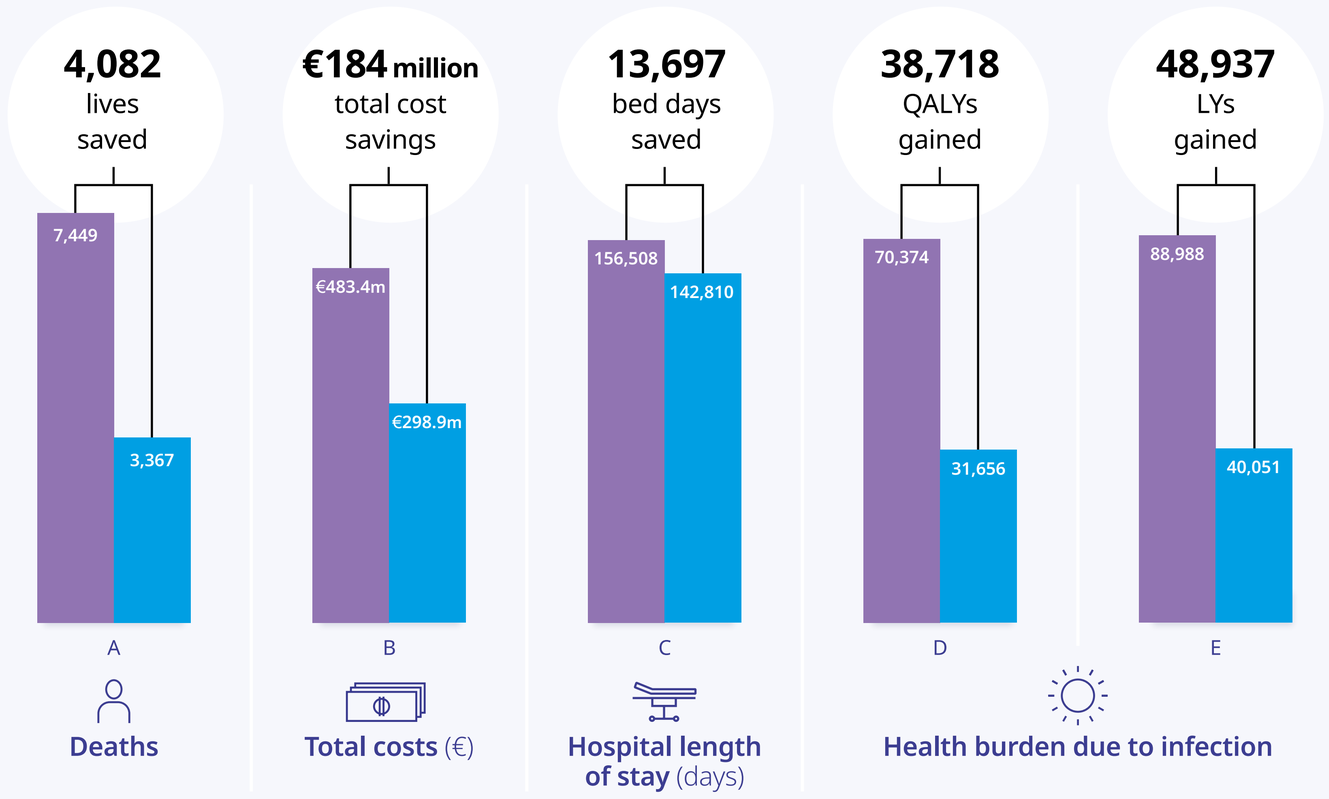


Figure 2. Absolute outcomes and incremental difference for **A)** Deaths **B)** Total costs **C)** Hospital length of stay **D)** QALYS and **E)** LYs lost to infection

Abbreviations: ATM-AVI, aztreonam-avibactam; LY, life years; QALY, quality-adjusted life years

At a willingness-to-pay threshold of €35,000,[8] compared with the current treatment strategy, introducing ATM-AVI was associated with a net monetary benefit of **€1.54 billion**, across the 10-year period and was **dominant** (i.e. cost saving and gained QALY)

Abbreviations
ATM-AVI, aztreonam-avibactam; cIAI, complicated intra-abdominal infection; HAP/VAP, hospital-acquired/ventilator-associated pneumonia; LOS, length of stay; LY, life years; MBL-PE, metallo-β-lactamase producing Enterobacterales; STEDI, spectrum, transmission, enablement, diversity, and insurance; QALY, quality-adjusted life year

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Disclosures
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