Cost-effectiveness analysis of introducing ceftazidime-avibactam to treatment strategies for hospital-acquired infections in Greece

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INTRODUCTION

- Antimicrobial resistance (AMR) represents a significant and growing health crisis, especially in Greece, where rates are among the highest in Europe[1]
- Ceftazidime-avibactam (CAZ/AVI) has been approved in Europe to treat a broad range of gram-negative bacterial infections, including complicated intra-abdominal infections (cIAI), complicated urinary tract infections (cUTI), hospital-acquired pneumonia (HAP) – including ventilator-associated pneumonia (VAP) – and gram-negative infections with limited treatment options (LTOi).[2] These infections pose an increasing threat to public health

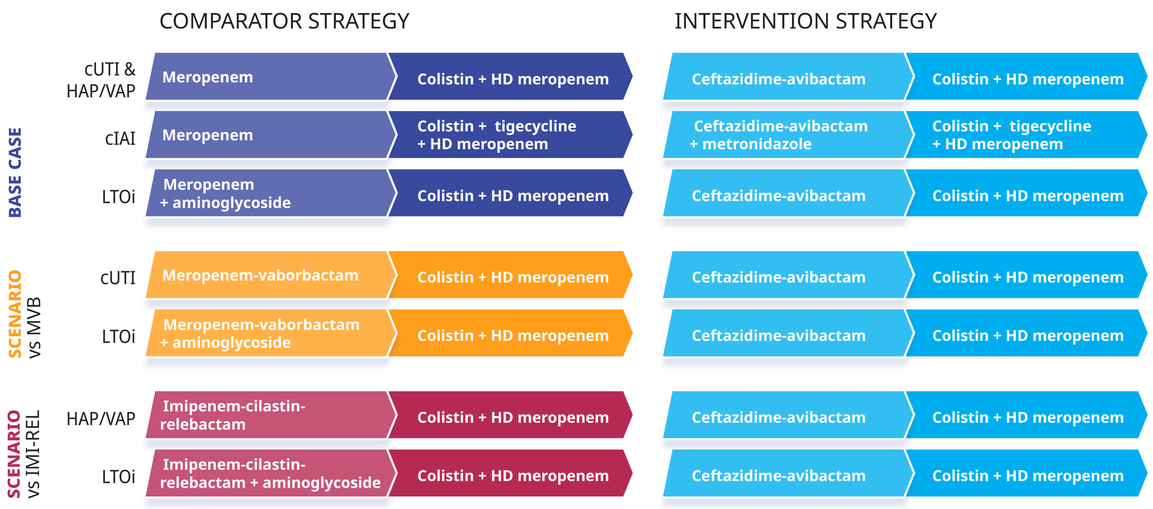
OBJECTIVE

- This cost-effectiveness analysis aimed at evaluating **CAZ/AVI** in the management of **gram-negative hospital-acquired infections (HAIs) in Greece**

METHODS

- A previsously published dynamic transmission model of AMR was adapted to the Greek setting.[3] The model considered HAIs across four different indications (cIAI, cUTI, HAP/VAP, and LTOi) caused by three gram-negative pathogens: *Escherichia coli*, *Klebsiella spp.*, and *Pseudomonas aeruginosa*
- **Treatment strategies:** The base case analysis considered a two-line, indication-specific, treatment strategy, where CAZ/AVI was compared with meropenem as the first-line therapies (Figure 1)

Figure 1: Treatment strategies



HD: high dose; IMI-REL: imipenem-cilastatin-relebactam; MVB: meropenem-vaborbactam.

- **Population size:** The model estimated outcomes based on a population size with an annual incidence of 27,508 HAIs, associated with the modelled indications and pathogens[4,5]
- **Efficacy:** Table 1 outlines inputs for treatment efficacy per indication and the baseline resistance of each treatment to the three modelled pathogens

Table 1: Treatment efficacy per indication and baseline resistance per pathogen

	TREATMENT EFFICACY PER INDICATION				BASELINE TREATMENT RESISTANCE LEVEL		
	cUTI	cIAI	HAP/VAP	LTOi	*E.coli*	*Klebsiella spp.*	*P. aeruginosa*
MEM	90.4%[6]	92.5%[7]	78.1%[8]	48.0%*[9]	3.0%[17]	75.0%[17]	46.0%[17]
CST + TGC + MEM (high dose)	NA	75%[10]	NA	NA	3.0%[18]	80.0%[18]	100.0%[18]
CST + MEM (high dose)	93.6%[11]	NA	58.0%[12]	54.0%[13]	3.0%[18]	75.0%[18]	46.0%[18]
CAZ/AVI	90.3%[4]	NA	77.4%[7]	85.0%[6]	0.0%	0.4%[19]	19.4%[20]
CAZ/AVI + MTZ	NA	91.7%[7]	NA	NA	0.0%	0.4%[19]	19.4%[20]
MVB	76.5%[14]	NA	NA	59.4%[15]	0.3%[18]	5.0%[18]	30.0%[18]
IMI-REL	NA	NA	61.0%[16]	61.0%[16]	0.3%[18]	7.1%[21]	15.8%[22]

* Meropenem + aminoglycoside
CAZ/AVI: ceftazidime-avibactam; CST: colistin; IMI-REL: imipenem-cilastatin-relebactam; MEM: meropenem; MTZ: metronidazole; MVB: meropenem-vaborbactam; TGC: tigecycline.

- **Resource use:** The model assumed a hospital length of stay (LOS) of 10 days for successful treatment and 5 days for unsuccessful treatment, before changing treatment. An additional 4 days LOS was assumed for patients who die
- **Adverse events:** The incidence of serious adverse events (SAEs) was estimated from the literature
- **Costs:** The associated medical costs were calculated as weighted averages of the SAEs reported in RECAPTURE (cUTI)[6] and RECLAIM (cIAI)[7] trials, using hospital costs from the Greek Diagnostic Related Groups (DRGs)[23]. The cost of an SAE is €1,121 for cUTI and €1,814 for cIAI. SAEs costs associated with treatment for cIAI were applied to HAP/VAP and LTOi indications
- Table 2 outlines additional inputs for utility and hospitalisation costs
- **Time horizon:** A ten-year infection transmission horizon was considered, where quality adjusted life years (QALYs) were estimated over a patient's lifetime, assuming a life-expectancy of 20.12 years (based on an average infected-population age of 65 years)[24]
- **Discounting rate and willingness-to-pay (WTP):** Costs and QALYs were discounted at a rate of 3.5%. QALYs were valued with a WTP threshold of €30,000–€35,000 per QALY

Table 2: Additional model inputs

Model input	cUTI	cIAI	HAP/VAP	LTOi
Utility (not infected)	0.79*[25]			
Utility (infected)	0.68[26]	0.60[27]	0.58[28]	0.60†
Daily hospitality costs	€195.50[23]	€281.80[23]	€328.15[23]	€269.50[23]

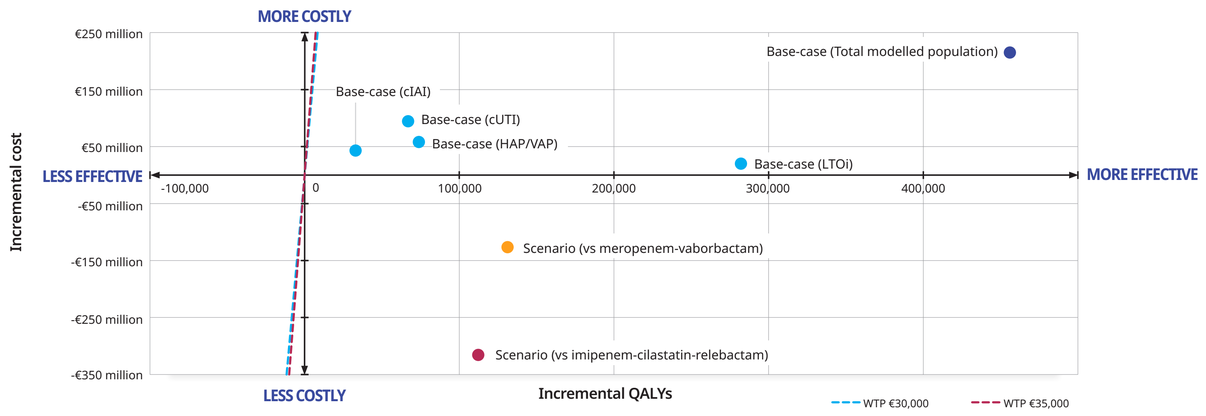
*Based on an average 65-year-old in Greece, assumed to be the average age of the infected population as validated by expert opinion
†Value assumed the same as cIAI

RESULTS

Base case analysis

- The intervention strategy, including CAZ/AVI, had an incremental cost-effectiveness ratio (ICER) of €471.16 per QALY when considering the total modelled population
- CAZ/AVI had the lowest ICER (€70.59) in treating LTOi (Figure 2)
- CAZ/AVI was estimated to save 46,606 lives over 10 years; furthermore, 337,361 hospital bed days and 55,184 SAEs were avoided. The intervention strategy also led to 150,935 fewer days on treatment (Figure 3)
- CAZ/AVI was associated with an additional 577,256 life years (LYs), equating to 456,062 QALYs versus the comparator strategy of the base case analysis

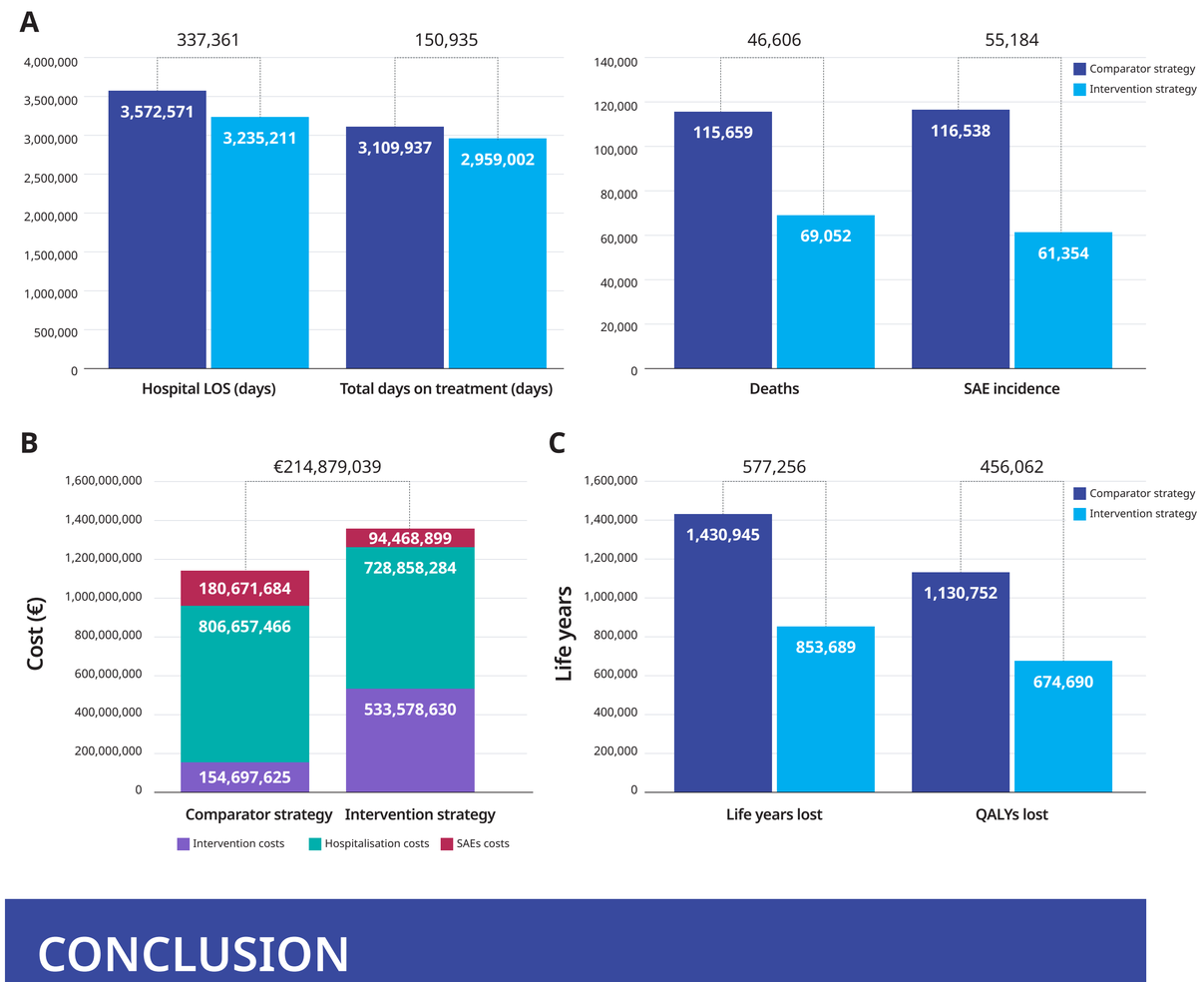
Figure 2: Cost-effectiveness plane of incremental costs and QALYs associated with CAZ/AVI vs comparators (base case [overall population and per indication] and scenarios)



Scenario analyses

- CAZ/AVI was dominant in both scenarios where comparator arms used MVB (cUTI and LTOi) and IMI-REL (HAP/VAP and LTOi) as the first-line treatment (Figure 2)
- MVB and IMI-REL were associated with 131,274 and 112,361 fewer QALYs, respectively, and were more costly (€126,643,948 and €315,719,230, respectively) than CAZ/AVI (Figure 2)

Figure 3: Health economic outcomes CAZ/AVI vs base case A) Clinical outcomes B) Incremental costs C) Incremental LYs and QALYs



CONCLUSION

- CAZ/AVI demonstrated considerable cost-effectiveness against comparators for treating gram-negative HAIs in Greece
- CAZ/AVI was dominant is scenarios compared with MVB and IMI-REL, where it was more effective and less costly
- As the value of new antimicrobials extend beyond those captured within this model, future methods should seek to estimate this additional value

DISCLOSURES

This analysis was supported by Pfizer Ltd. AT is an employee of Pfizer R&D UK. MB, VG, and AR are employees of Pfizer Hellas SA. JG, CP, RM and JD are employees of Health Economics and Outcomes Research Ltd. Health Economics and Outcomes Research Ltd. received fees from Pfizer Ltd. in relation to this study.

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