Cost-Effectiveness Of Ceftazidime-Avibactam Compared To Colistin For Treatment Of Carbapenem-Resistant Enterobacteriaceae Bacteremia And Pneumonia

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BACKGROUND

- Carbapenem-resistant *Enterobacteriaceae* (CRE) infections are an urgent public health threat and are associated with high mortality rates.
- Conventional therapy with colistin (COL) has poor efficacy and is associated with high rates of nephrotoxicity.
- Ceftazidime-avibactam (CAZ-AVI) is a novel β-lactam/β-lactamase inhibitor with activity against many CRE.
- Observational studies of CAZ-AVI suggest improved mortality and reduced risk of nephrotoxicity compared with COL; however, CAZ-AVI is significantly more expensive.

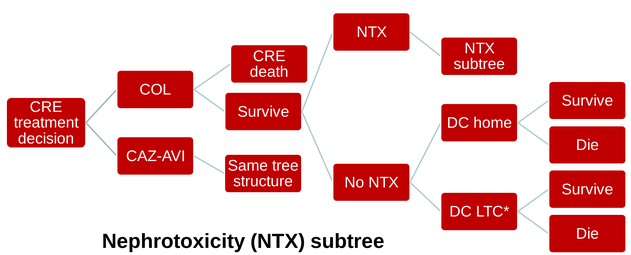
STUDY OBJECTIVE

- **To estimate the cost-effectiveness of CAZ-AVI compared with COL for treatment of CRE bacteremia and pneumonia**

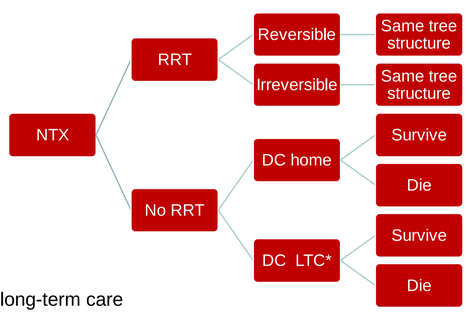
METHODS

- Decision analytic model from a healthcare system perspective with a 5-year time horizon
- Inputs derived from published sources
- Outcomes (discounted at 3% annually):
  - Costs (2017 $US)
  - Quality-adjusted life years (QALYs)
  - Incremental cost-effectiveness ratios (ICERs;$/QALY)
- ICERs compared to thresholds of $100,000/QALY and $150,000/QALY
- 1-way and probabilistic sensitivity analyses

Schematic of decision model



Nephrotoxicity (NTX) subtree



*LTC; long-term care

MODEL INPUTS

Input	Base case	Range
Probability values		
CRE attributable mortality (COL-based)		
BSI	0.401	0.2-0.6
Pneumonia	0.413	0.2-0.6
Absolute risk reduction with CAZ-AVI	0.23	0.09-0.35
Nephrotoxicity		
COL-based	0.42	0.2-0.6
CAZ-AVI-based	0.08	0.04-0.2
Nephrotoxicity requiring in-hospital RRT	0.052	0-0.2
Nephrotoxicity requiring chronic RRT	0.024	0-0.05
Discharge to long-term care	0.559	0.4-0.8
All-cause mortality, year 1		
Home	0.356	0.15-0.55
Long term care	0.479	0.2-0.6
All-cause mortality, year 2-5		
Home	0.112	0.05-0.2
Long term care	0.217	0.1-0.3
Relative risk of death on chronic RRT	3.15	2.78-3.58
Relative risk of discharge to long-term care with RRT	3.0	1.0-6.0
Costs (2017 $US)		
COL-based[a] (daily)	$235	+/- 50%
CAZ-AVI-based[a] (daily)	$1,038	+/- 50%
Nephrotoxicity		
Without RRT	$8,647	+/- 50%
With RRT	$23,013	+/- 50%
Chronic dialysis (annual)	$90,410	+/- 50%
Long-term care (annual)	$94,696	+/- 50%
Sepsis subsequent care		
Year 1	$24,709	+/- 50%
Years 2-5 (annual)	8,082	+/- 50%
Utilities[b]		
Home (recovered)	0.84	0.5-0.95
Hospitalization	0.73	0.4-1.0
Nephrotoxicity (reversible)	0.66	0.4-0.8
Long-term care	0.64	0.4-0.8
Chronic dialysis	0.59	0.4-0.8

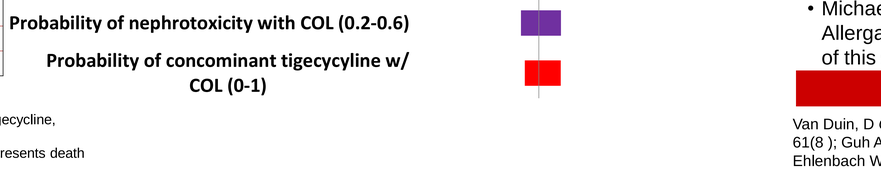
[a]Treatment costs were a weighted average of adjunctive therapies (i.e. tigecycline, meropenem, aminoglycoside) from observational studies
[b]Utilities represent health related quality of life on a 0-1 scale where 0 represents death and 1 represents perfect health

RESULTS

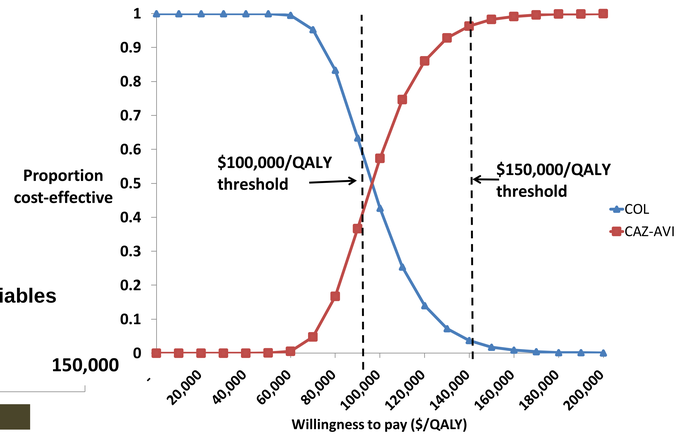
Cost-effectiveness of CAZ-AVI compared with COL for treatment of CRE pneumonia and bacteremia

Strategy	Cost	Incremental cost	Total QALYs	Incremental QALYs	ICER ($/QALY)
Colistin	109,400	----	1.26	-----	
CAZ-AVI	156,900	47,500	1.76	0.50	95,000

Tornado analysis depicting results of 1-way sensitivity analysis of key variables



Probabilistic sensitivity analysis results



LIMITATIONS

- CAZ-AVI effectiveness data based on limited observational studies
- Long term data on cost, quality of life and survival extrapolated from sepsis literature due to limited data specific to CRE
- Results may not apply in settings where carbapenem resistance mechanisms besides KPC are more prevalent

CONCLUSIONS

- **CAZ-AVI is a cost-effective treatment for CRE pneumonia and bacteremia at commonly accepted thresholds in the US**
- At a $100,000/QALY threshold, results were sensitive to:
  - Probability and cost of long-term care
  - Quality of life following CRE infection
  - CAZ-AVI's absolute risk reduction in mortality
  - All-cause mortality following recovery from CRE
  - Cost of CAZ-AVI
- At a $150,000/QALY threshold, results were robust to a wide range of plausible values for all model inputs

DISCLOSURES

- Michael Satlin has received research grant support from Allergan. Allergan had no role in the design, conduct or reporting of this study.

REFERENCES

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