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Early Health Outcomes Model on the Impact of Trimodulin in the Management of Patients with Severe Community-Acquired Pneumonia on Invasive Mechanical Ventilation Based on the CIGMA Phase 2 Randomized Placebo-Controlled Trial

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CONCLUSION:

Adding trimodulin to SoC reduces ICU LOS and mortality, leading to improved life expectancy, QALYs and evLYGs in patients with sCAP on IMV compared to SoC alone.

The effects are more pronounced in patients with inflammatory disease stage, indicated by CRP levels ≥70 mg/L.

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BACKGROUND

- Patients with severe community-acquired pneumonia (sCAP) often require intensive care unit (ICU) management and invasive mechanical ventilation (IMV), and have a high mortality risk[1]
- The phase II randomized placebo-controlled CIGMA trial indicated a potential mortality benefit when trimodulin was added to Standard of Care (SoC) in patients with sCAP on IMV (Twenty-eight-day all-cause mortality 22.2% [trimodulin] vs. 27.8% [placebo], p = 0.465)[2]
- Post-hoc analysis revealed a significant mortality benefit in patients with C-reactive protein (CRP) levels ≥70 mg/L before start of treatment (Twenty-eight-day all-cause mortality 13.8% [trimodulin] vs. 30.5% [placebo], p = 0.030)[2]

OBJECTIVE

- We developed a disease model for patients with sCAP on IMV to evaluate health outcomes of adjunctive trimodulin to SoC vs. SoC alone

METHODS

- A de novo model with short- and long-term components was developed using MS Excel. The starting age was 65 years

SHORT-TERM COMPONENT

- The short-term component, with a 28-day horizon, compared mortality, length of stay (LOS) in ICU and overall between treatment arms (Figure 1)
- Data from CIGMA populated the model, focusing on the overall population and the subpopulation with CRP levels ≥70 mg/L

Figure 1. Short-term Model

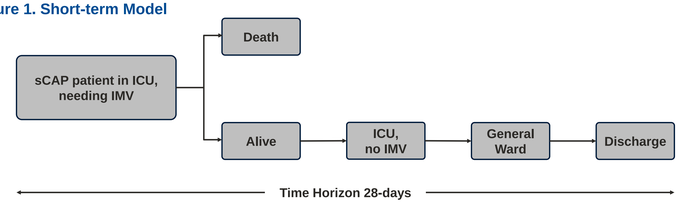
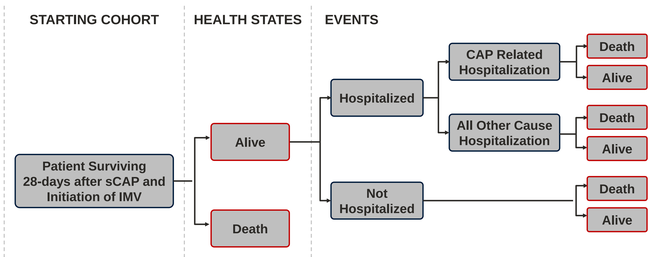


Figure 2. Long-term Model



LONG-TERM COMPONENT

- Survivors after 28 days entered the long-term component (20-year time horizon) with two Markov health states (alive and dead) using annual cycles (Figure 2)
- US-specific long-term mortality[3] (Table 1) and utilities[4] were sourced from literature
- Long-term outcomes included life expectancy (LE), quality-adjusted life years (QALY) and equal value of life-years gained (evLYG)
- A 3% discount rate was applied to health outcomes

Table 1. Long-term Mortality after CAP Relative to Control Subjects by Age[3]

Age	Events per 1000 patient-years	Adjusted HR (95% CI)
17-25	6	2.40 (1.30-4.43)
26-45	15	2.00 (1.65-2.43)
46-65	41	1.78 (1.58-2.00)
66-80	130	1.76 (1.62-1.91)
>80	261	1.42 (1.30-1.54)

CI=confidence interval; HR=hazard ratio

EQUAL VALUE OF LIFE-YEARS GAINED

- The equal value of life-years gained (evLYG) metric was introduced in 2018 by the Institute for Clinical and Economic Review (ICER) to address concerns raised by healthcare payers, patients, and advocacy groups on the QALY metric[5]
- ICER utilizes a value of 0.851 for the value of a healthy life year based on the age- and gender-adjusted utility of the healthy US population[5]
- The evLYG calculation was performed according to the following formula:

$$evLY\,A = QALY\,A/LY\,A * LY\,B + 0.851 * (LY\,A - LY\,B)$$
$$evLY\,B = QALY\,B$$
$$evLYG = evLY\,A - evLY\,B$$

RESULTS

SHORT TERM RESULTS

- In the overall population, trimodulin reduced mortality (-5.6%) and ICU LOS (-1.00 day), while total LOS increased (+0.50 days) (Table 2)
- In patients with CRP levels ≥70mg/L, trimodulin reduced mortality (-16.7%), ICU LOS (-0.47 days), and total LOS (-0.14 days) (Table 2)

LONG TERM RESULTS

- For the overall population, patients receiving trimodulin + SoC showed an increase in average LE of 0.80 years and a QALY improvement of 0.65 years compared to those receiving SoC alone (Table 3)
- In the subpopulation with CRP levels ≥70 mg/L, patients treated with trimodulin + SoC experienced an increase in average LE of 2.39 years and a QALY improvement of 1.93 years compared to those treated with SoC alone (Table 3)

Table 2. Short-term Results

	Trimodulin + SoC	SoC	Incremental
Overall Population			
Days in the ICU with IMV	12.80	13.80	-1.00
Days in the ICU	13.40	14.40	-1.00
Days in hospital	19.50	19.00	0.50
Survival	0.778	0.722	20%
CRP levels ≥70 mg/L			
Days in the ICU with IMV	13.25	13.84	-0.59
Days in the ICU	13.63	14.10	-0.47
Days in hospital	19.81	19.95	-0.14
Survival	0.862	0.695	55%

CRP=C-reactive protein; ICU=Intensive Care Unit; IMV=Invasive Mechanical Ventilation; SoC=Standard of Care

Table 3. Long-term Results

		Overall			CRP levels ≥70 mg/L		
		Trimodulin + SoC	SoC	Incremental	Trimodulin + SoC	SoC	Incremental
LY	Undiscounted	10.90	10.10	0.80	12.11	9.71	2.39
	Discounted	8.77	8.12	0.65	9.73	7.81	1.92
QALY	Undiscounted	8.79	8.14	0.65	9.76	7.83	1.93
	Discounted	7.09	6.57	0.52	7.87	6.31	1.56
	evLYG	7.12	6.57	0.55	7.95	6.31	1.64

CRP=C-reactive protein; evLYG=Equal value of life-years gained; LY=Life Years; QALY=Quality-adjusted Life years; SoC=Standard of Care

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