Cost-effectiveness of umeclidinium/vilanterol (UMEC/VI) versus glycopyrrolate/formoterol fumarate (GLY/FOR) in symptomatic patients with COPD in the UK: The AERISTO trial

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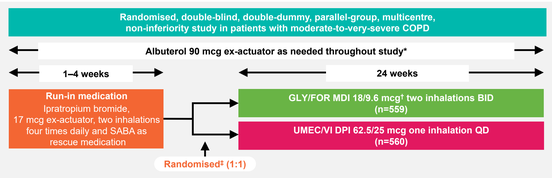
Introduction

- Healthcare utilisation and cost burden associated with COPD are substantial, with severity of symptoms and frequency of exacerbations being primary drivers.[1,2]
- The UK National Institute of Health and Care Excellence recommends dual long-acting bronchodilators as maintenance therapy for patients with COPD with persistent symptoms or exacerbations,[3] but further evidence is needed to evaluate the cost-effectiveness between dual bronchodilator therapies from a UK perspective.
- The AERISTO trial (NCT03162055; N=1,119) study design is shown in **Figure 1**.[4]
  - Co-primary endpoints: change from baseline in morning pre-dose trough FEV_1 over 24 weeks, and peak change from baseline in FEV_1 in 2 hours post dosing over 24 weeks.[4]
  - Results: GLY/FOR was non-inferior to UMEC/VI for treatment effect on peak FEV_1 and inferior for trough FEV_1.[4] (**Table 1**).
- Using data from the AERISTO trial, we assessed cost-effectiveness of UMEC/VI versus GLY/FOR from a UK NHS perspective.

Figure 1: **AERISTO study design**



Avoided within 6 h of spirometry testing; †equivalent to GLY/FOR 14.4/10 mcg; ‡stratification at randomisation based on COPD medications received at screening: SABA or LAMA or LABA or ICS alone vs dual therapies (LAMA/LABA or ICS/LABA).

Table 1: **Baseline characteristics and treatment effects inputs**

Parameter	Base-case input value (N=1,104)	Source
Demographics and baseline characteristics (pooled across both comparators)		
Female, %	27.4	AERISTO trial data*
Age, years, mean (SE)	64.1 (0.34)	AERISTO trial data*
BMI, %		
Low (<21)	9.5	EMAX trial data*
Medium (21–30)	58.4	Calculated
High (>30)	32.1	EMAX trial data*
Any CV comorbidity, %	43.5	EMAX trial data*
Any other comorbidity, %	54.6	EMAX trial data*
Prior history of ≥1 moderate exacerbation, %	47.9	AERISTO trial data*
mMRC score ≥2, %	39.9	EMAX trial data (assumed same as CAT score ≥21)*
Current smoker, %	53.5	AERISTO trial data*
Height, cm, mean (SE)	169.1 (0.19)	EMAX trial data*
Fibrinogen, μg/dL, mean (SE)	472.9 (2.37)	Predicted from risk equation[5]
Number of exacerbations in prior year, %		
Moderate exacerbations	86.3	UMEC/VI vs TIO/OLO trial data*
Severe exacerbations	13.7	UMEC/VI vs TIO/OLO trial data*
Baseline SGRQ score, mean (SE)	48.9 (0.55)	AERISTO trial data (CAT score converted to SGRQ)*†
Baseline FEV_1, % predicted, mean (SE)	46.1 (0.63)	AERISTO trial data*
6MWD, m, mean (SE)	48.7 (0.6)	Predicted from risk equation[5]
Treatment effects[4]	**GLY/FOR (n=552)**	**UMEC/VI (n=552)**
Trough FEV_1 change from baseline, mL (SE)	78.3 (10.1)	161.9 (10.1)
GLY/FOR vs UMEC/VI comparator mean difference (97.5% CI)		−83.6 (−111.8, −55.4)
CAT score change from baseline (SE)	−2.95 (0.20)	−3.51 (0.20)
UMEC/VI vs comparator mean difference (95% CI)		0.56 (0.06, 1.06)

Data not previously published; †CAT scores were observed and documented as a measure of patient's quality of life. As both CAT and SGRQ scores were collected in the EMAX trial, a regression equation was derived using pooled baseline data from EMAX. Slope and intercept from this regression equation were used to translate the AERISTO trial-observed CAT scores at baseline to an SGRQ measure.

Methods

Patient population

- This analysis was carried out using data from the AERISTO population.

Cost-effectiveness model

- The validated GALAXY-COPD model uses a linked risk equation approach to predict disease progression in terms of symptoms, exacerbations, lung function, and exercise capacity, as well as the associated healthcare costs, health-related quality of life and survival.[5,6]
  - Model risk equations were developed using data from a large patient cohort in the ECLIPSE study.[7]
  - A health state approach was used for healthcare costing.
- Probabilistic analyses were conducted to address the uncertainty in parameter estimation. Input parameters were assigned distributions that randomly sampled over 5,000 Monte Carlo simulations.

Model inputs

- Data on baseline characteristics and treatment effects from the AERISTO trial (**Table 1**) and 2022 UK healthcare cost data[8-11] (**Table 2**) were used to populate the GALAXY model.
  - Inputs for baseline parameters not available from the AERISTO trial were obtained from the EMAX trial (NCT03034915)[12] or UMEC/VI versus TIO/OLO (NCT02799784) study;[13] both of these trials evaluated the use of dual LAMA/LABA therapy in patients with COPD.
  - mMRC Dyspnoea Scale, 6MWD, fibrinogen, and SGRQ were not available directly from the trial data; therefore values for these parameters were estimated either using risk equations[7,12,14] or from analogous data collected in the trial.
- Base-case settings and assumptions are shown in **Table 3**.

Table 2: **Cost inputs***

Parameter	Base-case input value (N=1,104)		Source
	UMEC/VI	GLY/FOR	
Drug costs per day, £	1.08	1.08	BNF 2022[8]
Healthcare costs per year or per exacerbation, £			**Source**
Disease management, COPD severity (FEV_1, % predicted)			
Moderate to severe (50–80%)	128		NICE 2018[9]
Severe (30–<50%)	850		NICE 2018[9]
Very severe (<30%)	1,578		NICE 2018[9]
Exacerbation			
Moderate	88		NICE 2018[9]
Severe	2,379		NICE 2018[9]
Rescue medication costs			**Source**
OCS: prednisolone	1.04		NICE 2019[3]
Antibiotics			
Amoxicillin	0.06		NICE 2018[9]
Doxycycline	0.14		NICE 2018[9]
Clarithromycin	0.28		NICE 2018[9]

Unit costs were inflated to 2022 values using the Consumer Price Index data obtained from the Office of National Statistics.[11]

Table 3: **Base-case model settings and assumptions used in this study**

Base-case model settings	Assumptions
• UK NHS perspective	• Treatment effect was assumed to be persistent at a constant rate for all patients
• AERISTO trial population	• Treatment discontinuation was assumed to be zero in the first and subsequent years
• Lifetime horizon (probabilistic analysis)	• UMEC/VI treatment effects for FEV_1 were assumed to begin at the onset of the analysis (zero months)
• 1-year cycle length	
• 3.5% discount rate for costs and benefits	
• Treatment discontinuation and patient productivity costs excluded	

Scenario and sensitivity analysis

- Scenario analyses were conducted to examine the impact of alternative populations, assumptions, and model settings on the base-case model results.
- One-way sensitivity analyses were conducted on baseline covariate values that were not available from the trial data (i.e., where analogous data were used), and UMEC/VI treatment effects on SGRQ and FEV_1.

Results

Base-case probabilistic analysis

- Over a lifetime (25 years) horizon UMEC/VI was the dominant treatment, providing more QALYs at lower cost compared with GLY/FOR (**Table 4**).
- UMEC/VI provided an additional 0.354 LYs (95% range: 0.158, 0.592) and 0.203 QALYs (0.115, 0.310), versus GLY/FOR (**Table 4**).
- UMEC/VI resulted in cost savings of £862 (−£1,799, £47) versus GLY/FOR (**Table 4**).
- UMEC/VI showed higher QALYs in 100% of the simulations versus GLY/FOR (**Figure 2A**).
- At a willingness-to-pay threshold of £20,000 per QALY, the net probability that UMEC/VI was cost-effective was 100% versus GLY/FOR (**Figure 2B**).

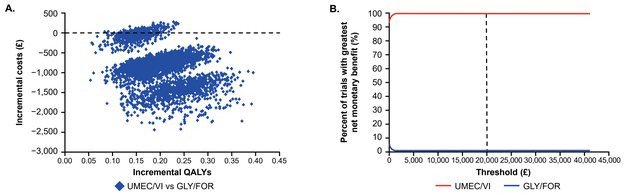
Scenario and sensitivity analyses

- In the scenario analysis, the incremental cost savings for UMEC/VI versus GLY/FOR at 5-year and 10-year time horizons were £912 and £913, respectively. In the scenario analysis where SGRQ treatment effect was excluded, the incremental cost saving for UMEC/VI versus GLY/FOR was £858.
- UMEC/VI was consistently the dominant treatment versus GLY/FOR across all scenario and sensitivity analyses.

Table 4: **Cost-effectiveness analyses for UMEC/VI versus GLY/FOR over a lifetime horizon**

Probabilistic analysis	UMEC/VI	GLY/FOR	Difference
Cumulative exacerbations			
Moderate	7.281	7.283	−0.002
Severe	2.234	2.348	−0.114
Total (moderate and severe)	9.515	9.631	−0.116
Severe PPPY	0.220	0.239	−0.020
Total PPPY	0.936	0.981	−0.046
Outcomes at end of timeframe			
Accumulated LYs, undiscounted (95% range)	10.167	9.814	0.354 (0.158, 0.592)
Accumulated QALYs (95% range)	5.478	5.275	0.203 (0.115, 0.310)
Costs			
Total costs, £	14,391	15,253	−862
Drug costs, £	3,324	3,229	94
Non-drug costs, £	11,067	12,024	−956
Incremental results			
Costs, £ (95% range)			−862 (−1,799, 47)
QALYs (95% range)			0.203 (0.115, 0.310)
ICER/QALY			Dominant

Figure 2: **Base-case for UMEC/VI versus GLY/FOR showing (A) incremental cost-effectiveness plane and (B) net benefit acceptability curve**



Conclusion

- Based on model predictions from a UK NHS perspective, symptomatic patients with moderate-to-very-severe COPD receiving UMEC/VI are expected to have better clinical and economic outcomes, including health-related quality of life and survival at lower costs versus GLY/FOR.
- Cost savings were predicted for UMEC/VI versus GLY/FOR, which resulted from lower maintenance and exacerbation costs.
- These findings suggest that UMEC/VI may reduce the economic burden of COPD relative to GLY/FOR in symptomatic patients with moderate-to-very-severe COPD and should be considered by physicians as a preferred treatment option in the UK.
- Limitations of this study include: 1-year discontinuation data were not available from AERISTO and as such discontinuation was excluded from the base-case; treatment effect on exacerbations in AERISTO was an exploratory endpoint and therefore effects on exacerbations are an indirect effect of differences in treatment effect on lung function and SGRQ.

Abbreviations

6MWD, 6-minute walk distance; BID, twice daily; BMI, body mass index; BNF, British National Formulary; CAT, COPD assessment test; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CV, cardiovascular disease; DPI, dry powder inhaler; FEV_1, forced expiratory volume in 1 second; FOR, formoterol fumarate; GLY, glycopyrrolate; ICER, incremental cost-effectiveness ratio; ICS, inhaled corticosteroids; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; LY, life-year; MDI, metered-dose inhaler; mMRC, modified Medical Research Council; NHS, National Health Service; OCS, oral corticosteroids; OLO, olodaterol; PPPY, per person per year; QALY, quality-adjusted life-year; QD, once daily; SABA, short-acting β_2-agonist; SE, standard error; SGRQ, St George's Respiratory Questionnaire; TIO, tiotropium; UMEC, umeclidinium; UK, United Kingdom; VI, vilanterol.

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Acknowledgements

Editorial support (in the form of writing assistance, including development of the initial draft based on author direction, assembling tables and figures, collating authors' comments, grammatical editing, and referencing) was provided by Alexandra Berry, PhD, at Fishawack Indicia Ltd., UK, part of Fishawack Health, and was funded by GSK.

Disclosures

This study was funded by GSK (Study 217635).
On behalf of all authors, an audio recording of this poster was prepared by **ASI** who did not receive any payment for this recording. **SGN** will be presenting this poster.
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