Cost-effectiveness of umeclidinium/vilanterol versus indacaterol/glycopyrronium in symptomatic patients with COPD in the UK

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Introduction

- Patients with COPD have high healthcare resource utilisation and treatment costs as a result of the significant morbidity and mortality they experience.[1]
- The UK NICE guidelines recommend dual long-acting bronchodilators as maintenance therapy for patients with COPD with persistent symptoms or exacerbations,[2] but more evidence is needed to evaluate the cost-effectiveness of available dual bronchodilator therapies in the UK; there are currently no head-to-head trial data available for comparison.
- A recent NMA investigated the efficacy of UMEC/VI versus IND/GLY LAMA/LABA dual therapies in symptomatic patients with COPD.[3]
  - The NMA included RCTs with a duration of at least 8 weeks testing lung function, HRQoL, breathlessness, rescue medication use, and exacerbations in symptomatic patients with COPD indexed on a LAMA/LABA dual therapy. A frequentist regression-based analysis was performed, with networks stratified by observation time horizon (12 and 24 weeks).[3]
  - UMEC/VI provided significantly greater improvements in trough FEV_1 at 24 weeks and in TDI focal score at 12 weeks versus IND/GLY. IND/GLY provided a significantly greater improvement in rescue medication use than UMEC/VI at 12 weeks. There was not a statistically significant difference between these dual therapies in SGRQ score, time to first exacerbation, or exacerbation rates.[3]
- Using data from the NMA, we assessed the cost-effectiveness of once-daily UMEC/VI 62.5/25 mcg versus once-daily IND/GLY 110/50 mcg for the treatment of COPD, from a UK NHS perspective.

Methods

Cost-effectiveness GALAXY model

- We used a validated linked risk equation model (GALAXY)[4] which predicts COPD disease progression (characterised by change from baseline in FEV_1, SGRQ, exercise capacity and incidence of exacerbations) and subsequent effects on healthcare costs, LYs and QALYs.
  - Model risk equations were developed and validated using data from a large patient cohort in the ECLIPSE study.[5]

Model inputs

- The COPD population parameters in the GALAXY model were set to pooled baseline data (across all comparator arms) from two studies comparing LAMA/LABA dual therapy: Study 204990 (NCT02799784)[6] for the base-case and the SPARK study[7] for the scenario analysis (**Table 1**). Data missing from SPARK were obtained from Study 204990.
  - Study 204990 was a randomised, two-period crossover open-label study that compared 8 weeks of treatment with UMEC/VI and TIO/OLO in patients with COPD.[6] It was selected because it reported the most complete set of baseline demographics data required to populate the GALAXY model from the studies in the NMA.
  - The SPARK study was a 64-week parallel-group study comparing treatment with IND/GLY versus GLY and TIO monotherapies.[7] It was used because it reported the data in a more severe COPD population than in Study 204990.

Table 1: Pooled baseline characteristics

Characteristic	Study 204990 (pooled data)	SPARK (pooled data)	Notes
Female, %	39.8	23.7	
Age, years, mean (SE)	64.4 (0.55)	63.1 (8.10)	
BMI, %			
Low (<21)	10.0	10.0	Data unavailable in SPARK, obtained from Study 204990
Medium (21–30)	50.0	50.0	Data unavailable in SPARK, obtained from Study 204990
High (>30)	40.0	40.0	Data unavailable in SPARK, obtained from Study 204990
Any CV comorbidity, %	27.0	27.0	Data unavailable in SPARK, obtained from Study 204990
Any other comorbidity, %	78.4	78.4	Data unavailable in SPARK, obtained from Study 204990
History of ≥1 exacerbation, %	19.0	98.0	
mMRC score ≥2, %	100.0	100.0	Data unavailable in SPARK, obtained from Study 204990
Current smokers, %	53.0	38.0	
Height, cm, mean (SE)	169.9 (0.60)	169.9 (0.60)	Data unavailable in SPARK, obtained from Study 204990
Fibrinogen, µg/dL, mean (SE)	453.2 (2.4)	488.5 (2.4)	Derived from a risk equation
6MWD, m, mean (SE)	349.9 (2.7)	308.2 (2.7)	Derived from a risk equation
Number of exacerbations in previous year, mean (SE)	0.18 (0.03)	0.18 (0.03)	Data unavailable in SPARK, obtained from Study 204990
Moderate exacerbations	0.16	0.16	Data unavailable in SPARK, obtained from Study 204990
Severe exacerbations	0.02	0.02	Data unavailable in SPARK, obtained from Study 204990
Starting FEV_1 % predicted, mean (SE)	59.6 (5.6)	37.0 (0.3)	
Starting SGRQ total score, mean (SE)	43.1 (1.00)	53.0 (0.67)	

- Treatment effects at 24 weeks on FEV_1, exacerbations, and SGRQ change from baseline were obtained from the NMA (**Table 2**).[3]

Table 2: Treatment effects

Parameter	UMEC/VI vs IND/GLY mean difference (95% CI)
FEV_1, change from baseline, mL	39.43 (19.56, 59.30)
SGRQ score, change from baseline	1.00 (−0.23, 2.24)
Moderate/severe exacerbations, relative risk	0.60 (0.32, 1.13)

Data obtained from the NMA.[3]

- Drug costs per day were identical for UMEC/VI and IND/GLY (**Table 3**).

Table 3: Cost inputs*

Parameter	UMEC/VI	IND/GLY	Source
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[2]
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.[10]*

- The outcomes modelled were cumulative total exacerbations, average annual exacerbations per patient per year, survival, QALYs, LYs, and incremental cost per QALY gained.
- The key base-case model assumptions were:
  - The Study 204990 population is representative of the UK COPD population likely to receive LAMA/LABA dual therapy.
  - Treatment effect was considered ongoing (persistent) until discontinuation. The efficacy of subsequent treatment (scenario analysis only) was assumed the same as the reference treatment in this analysis.
  - The treatment efficacy of exacerbation from the NMA was used for both moderate and severe exacerbation reductions in the model, assuming the treatment efficacy was the same for moderate and severe exacerbation.
  - Treatment discontinuation was assumed to be 0% for both treatment arms and a lifetime horizon was used.

Probabilistic analyses

- To address the uncertainty in parameter estimation, base-case probabilistic analyses were conducted. Input parameters were assigned distributions that randomly sampled over 5,000 Monte Carlo simulations.

Scenario and sensitivity analyses

- Scenario analyses were used to explore the effects of alternative populations, assumptions, and model settings on the base-case model results.
- One-way sensitivity analyses were performed on baseline covariate values not available from Study 204990, and UMEC/VI treatment effects on exacerbation, SGRQ and FEV_1.

Results

Deterministic base-case analysis

- Over a life-time horizon (25 years), UMEC/VI was the dominant treatment option, providing an additional 0.308 LYs and 0.038 QALYs compared with IND/GLY, and with cost savings of £1,874.
- UMEC/VI resulted in lower drug and healthcare costs than IND/GLY due to a lower utilisation of rescue medication and fewer exacerbations.

Probabilistic base-case analysis

- Over a life-time horizon (25 years), UMEC/VI was the dominant treatment option and provided an additional 0.307 (95% range: 0.107, 0.532) LYs and 0.036 (−0.106, 0.185) QALYs, with cost savings of £1,948 (−2,781, −1,242), versus IND/GLY (**Table 4**).

Table 4: Probabilistic base-case results

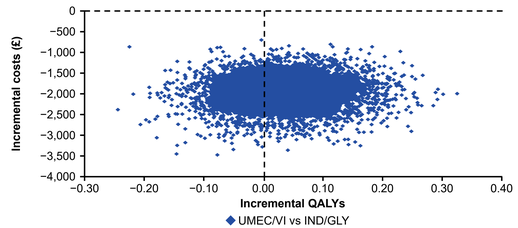
Probabilistic (25 years)	UMEC/VI	IND/GLY	Incremental
Cumulative number of exacerbations			
Moderate	3.493	5.618	−2.125
Severe	0.921	1.459	−0.538
Total	4.414	7.077	−2.663
Severe exacerbations PPPY	0.086	0.140	−0.054
Total exacerbations PPPY	0.411	0.679	−0.268
Outcomes at end of timeframe			
Survival at end of time horizon, %	1.2	0.9	0.32
Accumulated LYs (undiscounted)	10.731	10.424	0.307
Accumulated QALYs	5.836	5.801	0.036
Costs at end of timeframe, £			
Accumulated costs total	13,700	15,648	−1,948
Drug costs	8,657	9,136	−479
Total non-drug costs	5,043	6,512	−1,469
Incremental results			
Incremental cost, £			−1,948 (−2,781, −1,242)
Incremental LYs, undiscounted (95% range)			0.307 (0.107, 0.532)
Incremental QALYs (95% range)			0.036 (−0.106, 0.185)
ICER/QALY (vs IND/GLY)			Dominant (Dominant, Dominant)

- UMEC/VI was less costly and showed higher QALYs across most simulations versus IND/GLY. UMEC/VI remained the dominant treatment option compared with IND/GLY for 67% of 5,000 simulations (**Figure 1**).

Conclusion

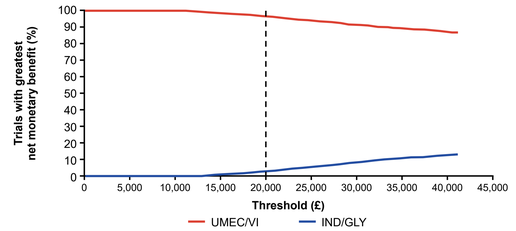
- A full set of patient characteristics was not available in Study 204990 and SPARK. These were predicted by risk equations or derived from analogous data, which can lead to overestimation of treatment effects.
- In a UK NHS setting, treatment with UMEC/VI was predicted to improve health outcomes and lower costs compared with IND/GLY in patients with symptomatic COPD.
- These findings suggest that UMEC/VI is a cost-effective treatment option for patients with COPD in the UK and should be considered by physicians as a preferred treatment option.

Figure 1: Base-case incremental cost-effectiveness plane



- At a willingness-to-pay threshold of £20,000 per QALY, the probability that UMEC/VI was cost-effective versus IND/GLY was 96% (**Figure 2**).

Figure 2: Base-case net-benefit acceptability curve



Scenario and sensitivity analyses

- UMEC/VI was the dominant treatment for all scenario analyses compared with IND/GLY, except for shorter time horizons (5 and 10 years).
- Across the sensitivity analyses, UMEC/VI was the dominant treatment option compared with IND/GLY except for the analyses including upper confidence interval for SGRQ or upper confidence interval for exacerbation treatment effects.
- Cost savings with UMEC/VI were highest in the scenario where patient productivity costs were included.

Abbreviations

6MWD, 6-minute walk distance; BMI, body mass index; BNF, British National Formulary; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; FEV_1, forced expiratory volume in one second; GLY, glycopyrronium; HRQoL, health-related quality of life; IND, indacaterol; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; LY, life-year; mMRC, modified Medical Research Council; NHS, National Health Service; NICE, National Institute of Health and Care Excellence; NMA, network meta-analysis; OCS, oral corticosteroids; OLO, olodaterol; PPPY, per person per year; QALY, quality-adjusted life year; RCT, randomised controlled trial; SE, standard error; SGRQ, St George's Respiratory Questionnaire; TDI, transition dyspnoea index; TIO, tiotropium; UK, United Kingdom; UMEC, umeclidinium; VI, vilanterol.

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