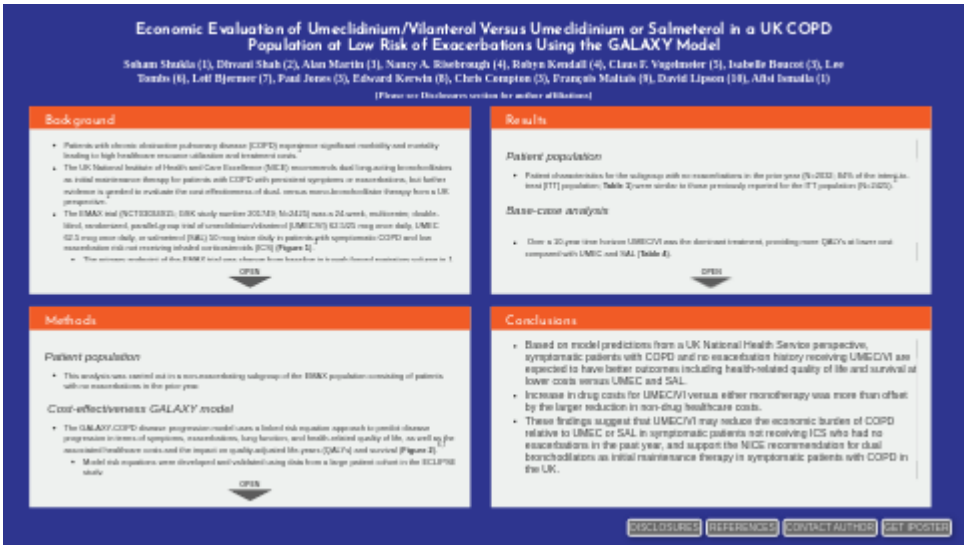
Economic Evaluation of Umeclidinium/Vilanterol Versus Umeclidinium or Salmeterol in a UK COPD Population at Low Risk of Exacerbations Using the GALAXY Model



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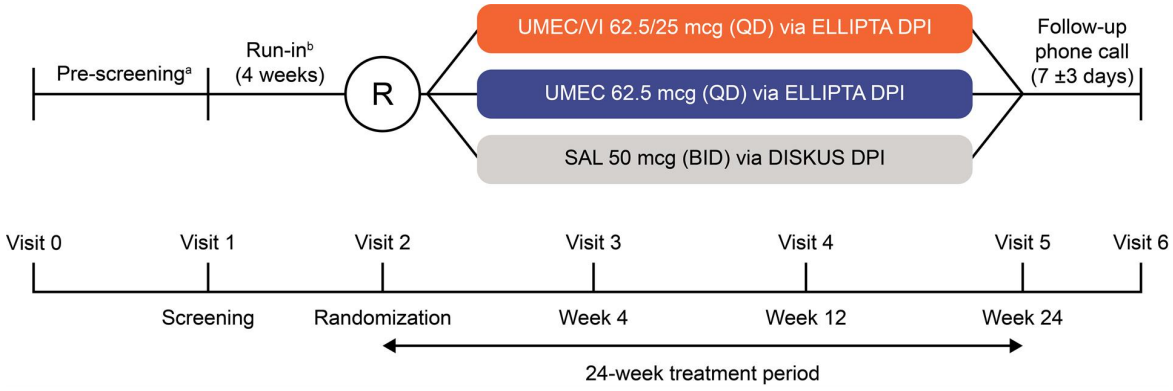
BACKGROUND

- Patients with chronic obstructive pulmonary disease (COPD) experience significant morbidity and mortality leading to high healthcare resource utilization and treatment costs.[1]
- The UK National Institute of Health and Care Excellence (NICE) recommends dual long-acting bronchodilators as initial maintenance therapy for patients with COPD with persistent symptoms or exacerbations, but further evidence is needed to evaluate the cost effectiveness of dual- versus mono-bronchodilator therapy from a UK perspective.[2]
- The EMAX trial (NCT03034915; GSK study number 201749; N=2425) was a 24-week, multicenter, double-blind, randomized, parallel-group trial of umeclidinium/vilanterol (UMEC/VI) 62.5/25 mcg once daily, UMEC 62.5 mcg once daily, or salmeterol (SAL) 50 mcg twice daily in patients with symptomatic COPD and low exacerbation risk not receiving inhaled corticosteroids (ICS) (**Figure 1**).[3]
  - The primary endpoint of the EMAX trial was change from baseline in trough forced expiratory volume in 1 second (FEV_1) at Week 24.[3]
  - EMAX demonstrated improved lung function and symptoms with UMEC/VI compared with UMEC or SAL in symptomatic patients with COPD at low risk of exacerbation not receiving ICS.[3]

Figure 1. EMAX study design.



Adapted from Maltais F, et al. *Respir Res* 2019;20:238. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/). [a]Pre-screening, existing bronchodilator maintenance therapy was limited to a LAMA or LABA, with patients required to be ICS and ICS/LABA free for ≥6 weeks and LAMA/LABA free for ≥2 weeks prior to run-in. In the ITT population, 69% of patients received LAMA or LABA monotherapy, while 31% received no COPD maintenance medication. [b]Patients were permitted to continue use of inhaled LAMAs or LABAs and/or study-provided as-needed salbutamol during the run-in period.

BID, twice daily; COPD, chronic obstructive pulmonary disease; DPI, dry powder inhaler; ITT, intent-to-treat; LABA, long-acting β2-agonist; LAMA, long-acting muscarinic antagonist; QD, once daily; R, randomization; SAL, salmeterol; UMEC, umeclidinium; VI, vilanterol.

- Using data from the EMAX trial, which recruited patients with <1 moderate and no severe COPD exacerbations in the previous year, we assessed cost effectiveness of UMEC/VI versus UMEC or SAL from a UK payer perspective in the subgroup of patients with no exacerbations in the prior year.
  - This subgroup was selected because COPD treatment guidelines recommend dual bronchodilator therapy for patients at low risk of future exacerbations,[2,4] and patients with no exacerbations in the prior year are at lower risk than those with 1 exacerbation in the prior year.[5] Furthermore, some symptomatic patients with a recent history of exacerbations may be expected to gain greater benefit from ICS-containing therapy.[4]

METHODS

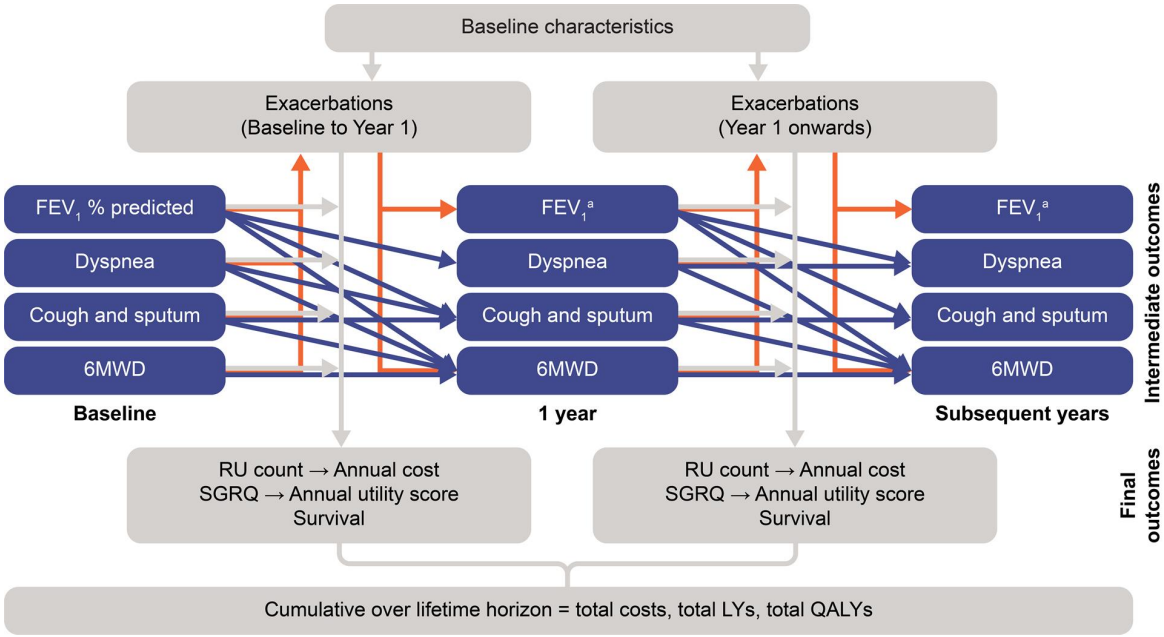
Patient population

- This analysis was carried out in a non-exacerbating subgroup of the EMAX population consisting of patients with no exacerbations in the prior year.

Cost-effectiveness GALAXY model

- The GALAXY-COPD disease progression model uses a linked risk equation approach to predict disease progression in terms of symptoms, exacerbations, lung function, and health-related quality of life, as well as the associated healthcare costs and the impact on quality-adjusted life-years (QALYs) and survival (**Figure 2**).[6,7]
  - Model risk equations were developed and validated using data from a large patient cohort in the ECLIPSE study.

Figure 2. Linked equations model.



Blue lines indicate the relationship between the central attributes in the different time periods. Orange lines indicate the relationship between intermediate outcomes and exacerbations. Gray lines indicate the relationship between the central attributes and the final health outcomes. Adapted from Briggs AH, et al. *Med Decis Making* 2017;37:469–80. https://doi.org/10.1177/0272989X16653118. Copyright © 2017 by the authors. Reprinted by permission of SAGE Publications, Inc.[14] [a]Calculated (in mL) using the risk equation at 1 year and converted to FEV_1% predicted based on the cohort profile.

6MWD, 6-minute walk distance; FEV_1, forced expiratory volume in 1 s; LY, life-year; QALY, quality-adjusted life-year; RU, resource utilization; SGRQ, St George's Respiratory Questionnaire.

Model inputs

- Data on baseline characteristics and treatment effects from the EMAX trial (**Table 1**) and 2020 UK healthcare cost data[7-12] (**Table 2**) were used to populate the GALAXY model.
  - Inputs for baseline parameters not available from the EMAX trial were set to predicted values based on risk equations (6-minute walk distance and fibrinogen) or analogous data (modified Medical Research Council dyspnea score; derived from COPD Assessment Test data).
  - SGRQ scores were converted to annual utility value using a published algorithm.[13]
  - A health state approach was used for healthcare costing.

- Base-case settings and assumptions are shown in **Table 3**.

Table 1. Demographics and baseline characteristics inputs.

Parameter	Base-case input value (subgroup with no exacerbations in prior 12 months; N=2032)			Source
Demographics and baseline characteristics (pooled across treatment arms)				
Female, %		40		EMAX trial data[a]
Age, years, mean (SD)		64.6 (8.4)		EMAX trial data[a]
BMI, %				
Low (<21)		9.7		EMAX trial data[a]
Medium (21–30)		58.0		EMAX trial data[a]
High (>30)		32.3		EMAX trial data[a]
Any CV comorbidity, %		45		EMAX trial data[a]
Any other comorbidity, %		55		EMAX trial data[a]
≥1 moderate exacerbation in prior year, %		0		Subgroup definition
mMRC score ≥2, %		40		EMAX trial data (assumed same as CAT score ≥21)[15]
Current smoker, %		51		EMAX trial data[a]
Height, cm, mean (SD)		169.5 (9.5)		EMAX trial data[a]
Fibrinogen, µg/dl, mean (SD)		453.4 (104.7)		Predicted from risk equation[a]
Number of exacerbations in prior year, mean		0		Subgroup definition
Severe exacerbations		0		Subgroup definition
Baseline SGRQ score, mean (SD)		44.72 (16.16)		EMAX trial data[a]
Baseline FEV_1 % predicted, mean (SD)		55.7 (12.8)		EMAX trial data[a]
6MWD, m, mean (SD)		385.3 (121.4)		Predicted from risk equation[a]
Treatment effects	**UMEC/VI (n=689)**	**UMEC (n=680)**	**SAL (n=663)**	
Trough FEV_1 at Week 24, ml (95% CI)				
LS mean CFB	128 (111, 145)	58 (40, 76)	−9 (−27, 9)	EMAX trial data[a]
UMEC/VI vs comparator mean difference	-	70 (45, 95) P<0.001	137 (112, 162) P<0.001	EMAX trial data[a]
SGRQ score at Week 24 (95% CI)				
LS mean CFB	−5.12 (−6.08, −4.16)	−5.02 (−6.02, −4.02)	−3.68 (−4.69, −2.68)	EMAX trial data[a]
UMEC/VI vs comparator mean difference	-	−0.10 (−1.49, 1.29) P=0.888	−1.44 (−2.83, −0.05) P=0.043	EMAX trial data[a]

[a]Data not previously published.
6MWD, 6-minute walk distance; BMI, body mass index; CAT, COPD Assessment Test; CFB, change from baseline; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; FEV_1, forced expiratory volume in 1 second; LS, least squares; mMRC, modified Medical Research Council; SAL, salmeterol; SD, standard deviation; SGRQ, St George's Respiratory Questionnaire; UMEC, umeclidinium; VI, vilanterol.

Table 2. Cost inputs.

Parameter	Base-case input value (subgroup with no exacerbations in prior 12 months; N=2032)			Source
	UMEC/VI (n=689)	**UMEC (n=680)**	**SAL (n=663)**	
Drug costs per day, £	1.08	0.92	0.81	BNF 2020[7]
Healthcare costs per year or per exacerbation, £[a]				
Disease management, COPD severity (FEV_1 % predicted)				
Moderate to severe (50–80%)		267		PSSRU 2019[9]; NHS 2018[10]; MIMS 2020[b]; NICE 2018[11]; Oostenbrink 2005[12]
Severe (30–<50%)		831		PSSRU 2019[9]; NHS 2018[10]; MIMS 2020[b]; NICE 2018[11]; Oostenbrink 2005[12]
Very severe (<30%)		2376		PSSRU 2019[9]; NHS 2018[10]; MIMS 2020[b]; NICE 2018[11]; Oostenbrink 2005[12]
Exacerbation				BNF 2020[7]; PSSRU 2019[9]; NHS 2018[10]; MIMS 2020[b]; NICE 2018[11]
Moderate		644		BNF 2020[7]; PSSRU 2019[9]; NHS 2018[10]; MIMS 2020[b]; NICE 2018[11]
Severe		6929		BNF 2020[7]; PSSRU 2019[9]; NHS 2018[10]; MIMS 2020[b]; NICE 2018[11]
Rescue medication costs	**UMEC/VI (n=689)**	**UMEC (n=680)**	**SAL (n=663)**	
Salbutamol inhalations/day	1.56	1.84	1.77	EMAX trial data[b]
Salbutamol cost per inhalation, £		0.06		BNF 2020[7]

[a]Costs were inflated to 2020 values using the Consumer Price Index. Physician fees and hospital costs were obtained from the 2018/19 PSSRU or the 2018/19 NHS National Cost Collection data. Medication costs were obtained from the MIMS and the BNF. [b]Data not previously published.
BNF, British National Formulary; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; MIMS, Monthly Index of Medical Specialties; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; PSSRU, Personal Social Services Research Unit; SAL, salmeterol; UMEC, umeclidinium; VI, vilanterol.

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

Scenario and sensitivity analyses

- Scenario analyses were conducted to examine the impact of assumptions and model settings on the base-case model results.
- Sensitivity analyses were performed to test the robustness of the base-case results for parameters not available from EMAX and for treatment effects (FEV_1 increment and St George's Respiratory Questionnaire [SGRQ] change).
- Probabilistic analyses were conducted to address the uncertainty in the parameters used within the model. Input parameters were assigned distributions that randomly sampled over 5000 Monte Carlo simulations.

RESULTS

Patient population

- Patient characteristics for the subgroup with no exacerbations in the prior year (N=2032; 84% of the intent-to-treat [ITT] population; **Table 1**) were similar to those previously reported for the ITT population (N=2425).[3]

Base-case analysis

- Over a 10-year time horizon UMEC/VI was the dominant treatment, providing more QALYs at lower cost compared with UMEC and SAL (**Table 4**).
- UMEC/VI provided an additional 0.090 LYs (95% range: 0.035, 0.158) and 0.055 QALYs (-0.059, 0.168) versus UMEC, and an additional 0.174 LYs (0.076, 0.286) and 0.204 QALYs (0.079, 0.326) versus SAL in the subgroup of patients with no exacerbations in the prior year (**Table 4**).
- UMEC/VI resulted in cost savings of £690 (-£1,306, -£231) versus UMEC and £1,336 (-£2,032, -£1,006) versus SAL in the subgroup of patients with no exacerbations in the prior year **(Table 4**).
- Over a 10-year horizon, UMEC/VI reduced non-drug costs by £1,106 versus UMEC and by £2,054 versus SAL, offsetting the smaller increase in drug costs in the subgroup of patients with no exacerbations in the prior year (**Table 4**).

Table 4. Cost-effectiveness analyses for UMEC/VI versus UMEC and SAL over a 10-year horizon.

Deterministic analysis	UMEC	UMEC/VI	Difference	SAL	UMEC/VI	Difference
Cumulative exacerbations						
Moderate	3.762	3.691	−0.071	3.762	3.622	−0.140
Severe	0.954	0.889	−0.064	0.954	0.831	−0.122
Total (moderate and severe)	4.716	4.580	−0.136	4.716	4.453	−0.263
Severe PPPY	0.119	0.109	−0.009	0.119	0.101	−0.017
Total PPPY	0.586	0.563	−0.023	0.586	0.542	−0.044
Health outcomes						
Survival, %	53.4	55.3	1.9	53.4	57.1	3.8
Accumulated LYs, undiscounted	8.05	8.14	0.09	8.05	8.22	0.17
Accumulated QALYs	4.79	4.84	0.06	4.79	4.99	0.20
Costs						
Total costs, £	13,850	13,160	−690	13,575	12,240	−1,336
Drug costs, £	2,670	3,086	416	2,396	3,114	719
Non-drug costs, £	11,180	10,074	−1,106	11,180	9,125	−2,054
Incremental results						
Costs, £ (95% range)			−690 (1,306, 231)			−1,336 (−2,032, −1,006)
LYs, undiscounted (95% range)			0.090 (0.035, 0.158)			0.174 (0.076, 0.286)
QALYs (95% range)			0.055 (-0.059, 0.168)			0.204 (0.079, 0.326)
ICER/QALY			Dominant[a]			Dominant[a]

[a]Dominant treatment provided greater QALYs at lower cost.
ICER, incremental cost-effectiveness ratios; LY, life-year; PPPY, per person per year; QALY, quality-adjusted life-year; SAL, salmeterol; UMEC, umeclidinium; VI, vilanterol.

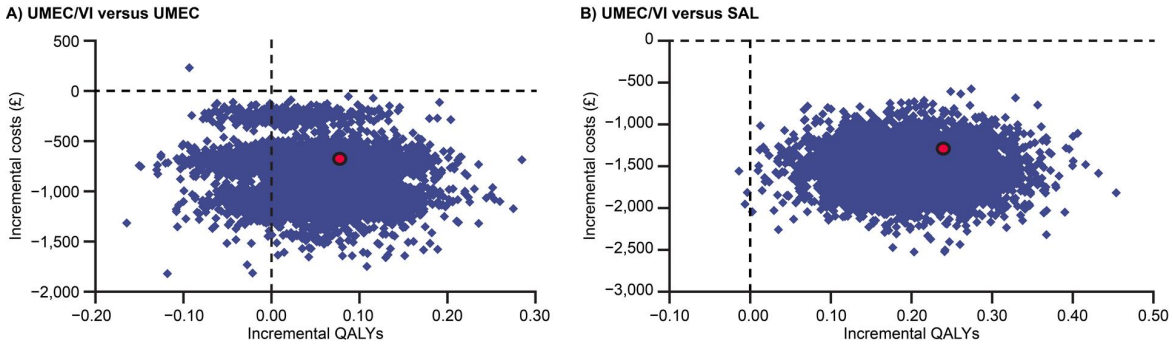
Scenario and sensitivity analyses

- Incremental cost-effectiveness ratios (ICERs) for UMEC/VI versus UMEC were sensitive to time horizon (5-year time horizon; ICER per QALY: £4) and SGRQ treatment effect (input value: confidence interval upper bound [1.4]; ICER per QALY: £12,337).
- UMEC/VI was consistently the dominant treatment versus SAL costs in the subgroup of patients with no exacerbations in the prior year.

Probabilistic analysis

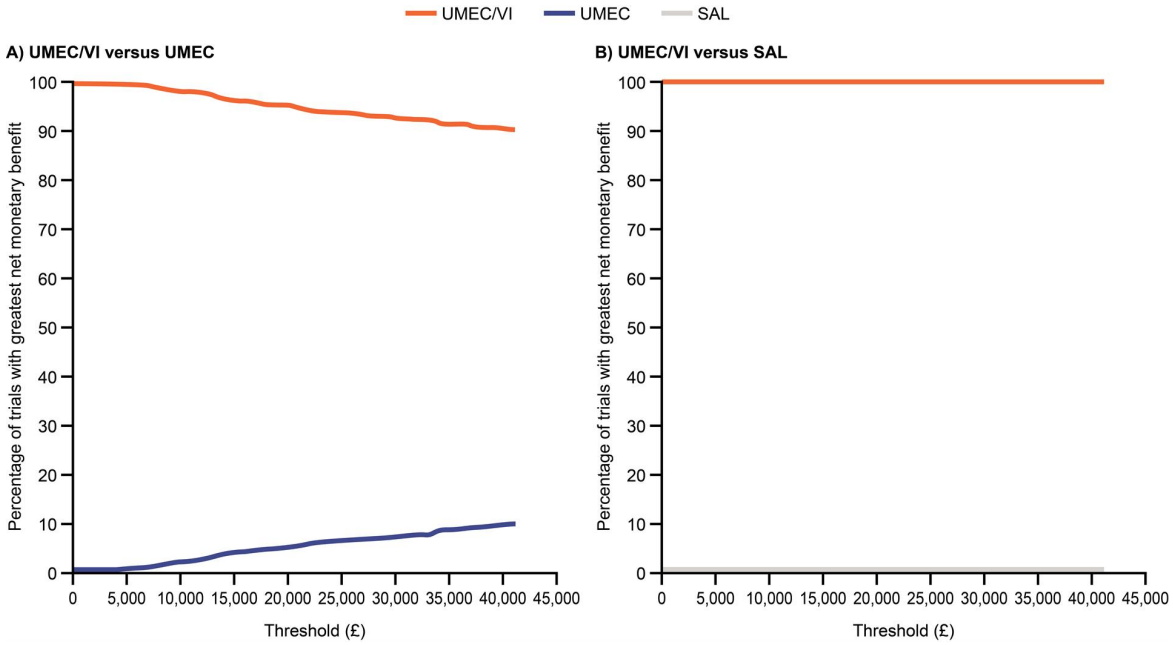
- UMEC/VI was less costly than UMEC or SAL across all simulations.
- UMEC/VI showed higher QALYs in 82% of the simulations versus UMEC (**Figure 3A**) and in 99% of the simulations versus SAL (**Figure 3B**).
- At a willingness-to-pay threshold of £20,000 per QALY, the net probability that UMEC/VI was cost effective was 95% versus UMEC (**Figure 4A**) and 100% versus SAL (**Figure 4B**) costs in the subgroup of patients with no exacerbations in the prior year.

Figure 3. Probabilistic analysis of incremental cost effectiveness with (A) UMEC/VI versus UMEC and (B) UMEC/VI versus SAL.



QALYs, quality-adjusted life-years; SAL, salmeterol; UMEC, umeclidinium; VI, vilanterol.

Figure 4. Net benefit acceptability curves for with (A) UMEC/VI versus UMEC and (B) UMEC/VI versus SAL.



SAL, salmeterol; UMEC, umeclidinium; VI, vilanterol.

CONCLUSIONS

- Based on model predictions from a UK National Health Service perspective, symptomatic patients with COPD and no exacerbation history receiving UMEC/VI are expected to have better outcomes including health-related quality of life and survival at lower costs versus UMEC and SAL.
- Increase in drug costs for UMEC/VI versus either monotherapy was more than offset by the larger reduction in non-drug healthcare costs.
- These findings suggest that UMEC/VI may reduce the economic burden of COPD relative to UMEC or SAL in symptomatic patients not receiving ICS who had no exacerbations in the past year, and support the NICE recommendation for dual bronchodilators as initial maintenance therapy in symptomatic patients with COPD in the UK.

DISCLOSURES

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- Dhvani Shah is an ICON employee and holds shares and stocks in ICON.
- Alan Martin is a GSK employee and holds shares and stocks in GSK.
- Nancy A. Risebrough is an ICON employee and holds shares and stocks in ICON.
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