Economic Analysis of New Single-Inhaler Triple Therapies in Patients with COPD in the UK

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Cai R,[1] Martin A,[2] Ge Y,[3] Risebrough NA,[3] Sharma R,[4] Haeussler K,[5] Compton C,[4] Halpin DMG,[6] Ismaila AS[7,8]

[1]ICON Health Economics, ICON plc, Amsterdam, The Netherlands; [2]Value Evidence and Outcomes, GSK, Brentford, UK; [3]ICON Health Economics, ICON plc, Toronto, ON, Canada; [4]Global Medical, GSK, Brentford, UK; [5]ICON Health Economics, ICON plc, Munich, Germany; [6]University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter, UK; [7]Value Evidence and Outcomes, GSK, Collegeville, PA, USA; [8]Department of Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most costly inpatient conditions treated by the United Kingdom (UK) National Health Service[1]

Triple therapy (inhaled corticosteroid [ICS], long-acting β_2-agonist [LABA] and long-acting muscarinic antagonist [LAMA]) is recommended for patients with COPD who remain symptomatic or at risk of exacerbation despite dual maintenance therapy (ICS/LABA or LAMA/LABA)[2]

Triple therapy via multiple inhalers was previously the only option; however, single-inhaler triple therapies (SITTs) have now been developed

Although the cost-effectiveness of SITTs versus different dual maintenance therapies or multiple-inhaler triple therapies has previously been assessed,[3–5] the cost-effectiveness of individual SITTs versus other SITTs is yet to be examined

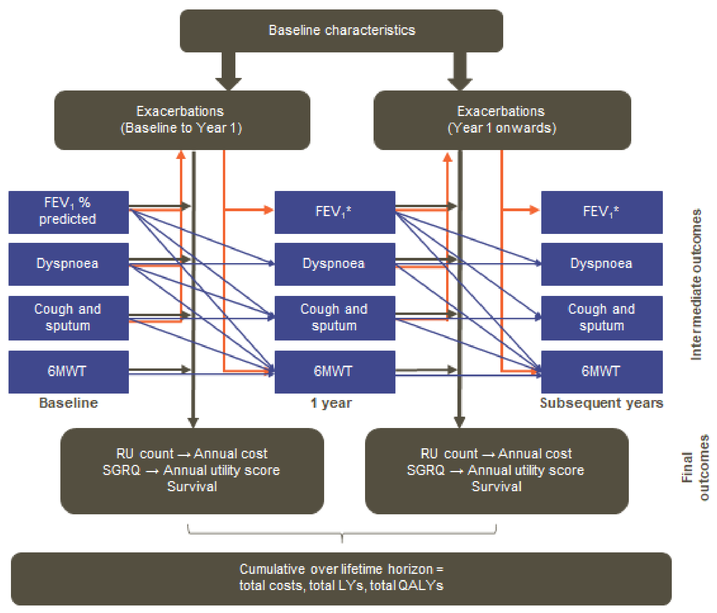
Aims

This study assessed the cost-effectiveness of SITT with fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) versus other SITTs (budesonide/glycopyrronium/formoterol [BUD/GLY/FOR] and beclomethasone dipropionate [BDP]/FOR/GLY) for the treatment of patients with moderate-to-severe COPD inadequately controlled with dual maintenance therapy, in a lifetime horizon from a UK healthcare perspective

Methods

- Analysis conducted using the validated GALAXY COPD model,[6] which employs linked risk equations to model associations between patient characteristics, treatment effects, disease progression and outcomes (**Figure 1**)
- Efficacy estimates were derived from a frequentist network meta-analysis (NMA), which compared FF/UMEC/VI with SITTs BUD/GLY/FOR (320/18/9.6), BUD/GLY/FOR (160/18/9.6) and BDP/FOR/GLY (100/6/12.5).[7] SITT trials included in the NMA are shown in **Table 1**
- The baseline characteristics of patients in SITT studies included in the NMA are summarised in **Table 1**. In the base case, the model was populated using baseline characteristics from the IMPACT trial[8]
- UK healthcare resource unit and drug costs were applied, with costs (2022 Great British Pounds) and health outcomes (except for life years [LYs]) discounted at 3.5% annually
- The analysis was probabilistic with a lifetime horizon. Deterministic scenario and sensitivity analyses were conducted to assess the robustness of the results

Figure 1. GALAXY model



Purple lines indicate the relationship between the central attributes in the different time periods. Orange lines indicate the relationship between intermediate outcomes and exacerbations. Grey lines indicate the relationship between the central attributes and the final health outcomes
*Calculated (in mL) using the risk equation at 1 year and converted to FEV_1% predicted based on the cohort profile
6MWT, 6-minute walk test; FEV_1, forced expiratory volume in 1 second; LY, life year; QALY, quality-adjusted life year; RU, resource utilisation; SGRQ, St. George's Respiratory Questionnaire
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Table 1. SITT trials included in the NMA

	IMPACT[8]	FULFIL[9]	200812[10]	KRONOS[11]	ETHOS[12]	TRISTAR[13]	TRIBUTE[14]	TRILOGY[15]
Treatment arms*	FF/UMEC/VI (100/62.5/25) vs FF/VI (100/25) vs UMEC/VI (62.5/25)	FF/UMEC/VI (100/62.5/25) vs BUD/FOR (400/12)	FF/UMEC/VI (100/62.5/25) vs UMEC (62.5) + FF/VI (100/25)	BUD/GLY/FOR (320/18/9.6) vs GLY/FOR (18/9.6) vs BUD/FOR (320/9.6) vs BUD/FOR (400/12)	BUD/GLY/FOR (320/18/9.6) vs BUD/GLY/FOR (160/18/9.6) vs GLY/FOR (18/9.6) vs BUD/FOR (320/9.6)	BDP/FOR/GLY (100/6/12.5) vs FF/VI (100/25) + TIO (18)	BDP/FOR/GLY (87/5/9) vs IND/GLY (85/43)	BDP/FOR/GLY (100/6/12.5) vs BDP/FOR (100/6)
Population size	10 355	1810	1055	1896	8509	1157	1532	1367
Gender, female (%)	34.0	25.9	25.6	28.8	40.3	24.5	28.0	24.2
Age (years)	65.3	63.9	66.3	65.2	64.6	63.9	64.5	63.5
History of ≥1 exacerbation (%)	99.91	65.19	100.00	25.58	99.90	NR	100.00	100.00
BMI low, <21 (%)	17.00	6.81	15.3	20.9	15.0	NR	16.4	15.9
BMI med, 21–30 (%)	58.00	68.25	59.0	51.6	50.9	NR	60.3	59.4
BMI high, >30 (%)	25.00	24.93	25.7	27.5	34.1	NR	23.3	24.7
mMRC score ≥2 (%)	37	42.65	42.67	33.7	NR	44.5	NR	48.6
Current smoker (%)	35	43.87	38.01	39.56	41.07	NR	44.54	47.00
Starting FEV_1 predicted (%)	45.50	45.30	45.00	50.25	43.40	NR	NR	NR
Resulting FEV_1	1215	1282	1205	NA	NA	NA	1070	1110

*Numbers in brackets denote drug concentrations in µg
BDP, beclomethasone dipropionate; BMI, body mass index; BUD, budesonide; FEV_1, forced expiratory volume in 1 second; FF, fluticasone furoate; FOR, formoterol; GLY, glycopyrronium bromide; IND, indacaterol; mMRC, modified Medical Research Council; NA, not available; NMA, network meta-analysis; NR, not reported; SITT, single-inhaler triple therapy; TIO, tiotropium; UMEC, umeclidinium bromide; VI, vilanterol

Methods

Table 2. Model inputs: treatment effects

Comparator treatment (24 weeks analysis)	FF/UMEC/VI versus comparator, mean difference (95% CI)		
	Change from baseline in FEV_1 (mL)	Change from baseline in SGRQ†	Relative risk for moderate and severe exacerbations
BUD/GLY/FOR (320/18/9.6)	111.22 (79.80, 142.63)	–0.69 (–2.56, 1.18)	0.62 (0.45, 0.86)
BUD/GLY/FOR (160/18/9.6)	110.77 (71.78, 149.76)	–0.90 (–2.83, 1.02)	0.61 (0.44, 0.85)
BDP/FOR/GLY*	46.70 (15.21, 78.20)	–1.43 (–3.47, 0.61)	0.73 (0.51, 1.04)

*12 weeks analysis available only. †A decrease in SGRQ represents an improvement in heath-related quality of life
BDP, beclomethasone dipropionate; BUD, budesonide; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; FF, fluticasone furoate; FOR, formoterol; GLY, glycopyrronium bromide; SGRQ, St. George's Respiratory Questionnaire; UMEC, umeclidinium bromide; VI, vilanterol

Results

Results for FF/UMEC/VI showed gains in both LYs and quality-adjusted LYs (QALYs) together with cost savings compared to all three comparators in the analysis BUD/GLY/FOR (320/18/9.6), BUD/GLY/FOR (160/18/9.6) and BDP/FOR/GLY (**Table 3**)

Table 3. Base case analysis (probabilistic)

Lifetime horizon	Comparator	FF/UMEC/VI	Incremental (95% CI) FF/UMEC/VI vs comparator
BUD/GLY/FOR (320/18/9.6)			
Accumulated LYs (undiscounted)	8.861	9.478	0.617 (0.271, 1.010)
Accumulated QALYs	4.453	4.739	0.286 (0.096, 0.490)
Accumulated total costs	£18 322	£16 705	–£1618 (–£3171, £148)
ICER/QALY gained			**Dominant***
BUD/GLY/FOR (160/18/9.6)			
Accumulated LYs (undiscounted)	8.899	9.526	0.626 (0.258, 1.044)
Accumulated QALYs	4.464	4.769	0.305 (0.093, 0.536)
Accumulated total costs	£18 417	£16 707	–£1710 (–£3342, –£235)
ICER/QALY gained			**Dominant***
BDP/FOR/GLY			
Accumulated LYs (undiscounted)	8.899	9.229	0.330 (0.071, 0.656)
Accumulated QALYs	4.464	4.695	0.232 (0.035, 0.439)
Accumulated total costs	£18 419	£17 196	–£1223 (–£2844, £428)
ICER/QALY gained			**Dominant***

*Greater benefit at lower cost
BDP, beclomethasone dipropionate; BUD, budesonide; CI, confidence interval; FF, fluticasone furoate; FOR, formoterol; GLY, glycopyrronium bromide; ICER, incremental cost-effectiveness ratio; LY, life year; QALY, quality-adjusted life year; UMEC, umeclidinium bromide; VI, vilanterol

Incremental cost-effectiveness

FF/UMEC/VI was the dominant treatment option in 98%, 99%, and 94% of probabilistic analysis iterations versus BUD/GLY/FOR (320/18/9.6), BUD/GLY/FOR (160/18/9.6), and BDP/FOR/GLY, respectively

Figure 2. Probabilistic analysis incremental cost-effectiveness

BDP, beclomethasone dipropionate; BUD, budesonide; FF, fluticasone furoate; FOR, formoterol; GLY, glycopyrronium bromide; QALY, quality-adjusted life year; UMEC, umeclidinium bromide; VI, vilanterol

At a willingness to pay threshold of £20 000, the probability of FF/UMEC/VI being cost-effective was 100%, 100% and 99.58% versus BUD/GLY/FOR (320/18/9.6), BUD/GLY/FOR (160/18/9.6) and BDP/FOR/GLY, respectively

Deterministic scenario and sensitivity analyses

- FF/UMEC/VI remained the dominant option across all scenario and sensitivity analyses, except for one analysis where the most pessimistic treatment effect on exacerbation reduction versus BDP/FOR/GLY was assumed, resulting in an incremental cost-effectiveness ratio of £2780/QALY
- Results were most sensitive to treatment effect on exacerbations and St George's Respiratory Questionnaire score

Study limitations

Certain differences existed in the study design and inclusion/exclusion criteria of the trials included in the analyses. The robustness of the analyses due to varying baseline characteristics were assessed in various sensitivity analyses

Conclusion

Based on this analysis of SITT trials, FF/UMEC/VI is a dominant treatment option compared with BUD/GLY/FOR (both dosages) and BDP/FOR/GLY for the treatment of patients with COPD in the UK

Disclosures

The authors declare the following real or perceived conflicts of interest during the last three years in relation to this presentation:
- ASI, RS, AM, and CC are employees of GSK and/or hold stocks/shares in GSK. ASI is also an unpaid faculty member at McMaster University.
- NAR, YG, RC, and KH are employees of ICON plc. ICON plc. received funding from GSK to conduct this study.
- DMG reports personal fees from AstraZeneca, personal fees and non-financial support from Boehringer Ingelheim, personal fees from Chiesi and GSK, personal fees and non-financial support from Novartis, and personal fees from Pfizer and Sanofi

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Author email address: Rui.Cai@iconplc.com

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