Economic benefit of FF/UMEC/VI by baseline blood EOS count in COPD in the UK - The IMPACT trial

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Digital poster
Narrated summary

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Introduction

- COPD is a leading cause of morbidity and mortality worldwide[1]
- Exacerbations of COPD are a key driver of the clinical and economic burden of the disease[2]
- The phase 3, randomised, double-blind, 52-week global IMPACT trial demonstrated that once-daily single-inhaler triple therapy (FF/UMEC/VI) significantly reduced exacerbations compared with dual therapies (FF/VI or UMEC/VI)
  - Subsequent analysis also showed greater treatment effects for use of inhaled corticosteroids in patients with COPD with increased blood EOS count[4]
- The study aimed to assess long-term incremental cost-effectiveness of FF/UMEC/VI vs FF/VI and UMEC/VI by baseline blood EOS count, from a UK NHS perspective, using IMPACT data[3]

Methods

Model structure and inputs

- A probabilistic analysis was performed using the GALAXY COPD model – a disease progression model which employs a novel linked risk equation to model associations between patient characteristics, treatment effects and outcomes[5]
- Baseline characteristics and treatment effects for subgroups, defined by baseline EOS count cut points of 100, 150 and 300 µL, were identified from IMPACT and used in the model **(Table 1)**
- Related health costs were also used as model inputs, including drug cost per day (FF/UMEC/VI, £1.48; FF/VI, £0.73; UMEC/VI, £1.08), health state management costs per year (moderate-to-severe, £128; severe, £850; very severe, £1578) and management cost per exacerbation (moderate, £88; severe, £2378)[6,7]

Table 1: **Baseline characteristics and treatment effects by baseline blood EOS count**

Parameters	Overall (ITT, N=10 355)	EOS <0.10 10⁹/L (N=2591)	EOS ≥0.10 10⁹/L (N=7742)	EOS <0.15 10⁹/L (N=4482)	EOS ≥0.15 10⁹/L (N=5851)	EOS <0.30 10⁹/L (N=8089)	EOS ≥0.30 10⁹/L (N=2244)
Baseline characteristics							
Female, %	34.0	36.8	32.6	36.7	31.3	35.2	28.2
Age, years (SE)	65.3 (0.1)	65.5 (0.2)	65.2 (0.1)	65.5 (0.1)	65.1 (0.1)	65.3 (0.1)	65.1 (0.2)
BMI low, %	17.0	20.4	16.1	19.2	15.6	17.2	17.1
BMI med, %	58.0	56.6	58.0	56.8	58.3	57.3	59.1
BMI high, %	25.0	23.0	26.0	24.0	26.1	25.6	23.8
Any CVD comorbidity, %	44.0	43.6	44.1	44.5	43.5	44.4	42.3
Any other comorbidity, %	57.0	56.4	57.1	56.6	57.1	57.2	55.8
History of ≥1 exacerbation, %	100.0	100.0	100.0	100.0	100.0	100.0	100.0
mMRC score ≥2, %	37.0	35.6	36.8	36.2	36.7	36.5	36.5
Current smoker, %	35.0	36.5	34.0	35.2	34.2	34.9	33.5
Height, cm (SE)	167.5 (0.1)	166.6 (0.2)	167.8 (0.1)	166.9 (0.1)	167.9 (0.1)	167.4 (0.1)	168.0 (0.2)
Number of exacerbations in previous year, mean (SE)	1.7 (0.0)	1.7 (0.0)	1.7 (0.0)	1.7 (0.0)	1.7 (0.0)	1.7 (0.0)	1.8 (0.0)
Moderate exacerbations, prior year %	1.4	1.4	1.4	1.4	1.4	1.4	1.5
Severe exacerbations, prior year %	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Starting SGRQ-c, total score (SE)	50.7 (0.3)	50.6 (0.3)	50.7 (0.2)	50.7 (0.3)	50.6 (0.2)	50.7 (0.2)	50.5 (0.4)
Starting FEV_1% predicted, % (SE)	45.5 (0.2)	44.7 (0.3)	45.8 (0.2)	45.0 (0.2)	45.9 (0.2)	45.2 (0.2)	46.7 (0.3)
Treatment effects							
FEV_1 increment, mean mL difference (SE or 95%CI)							
FF/UMEC/VI vs FF/VI	97.0 (85.0, 109.0)	82.0 (11.8)	102.0 (7.1)	103.0 (8.8)	93.0 (8.4)	100.0 (6.6)	91.0 (15.0)
FF/UMEC/VI vs UMEC/VI	54.0 (39.0, 69.0)	40 (14.5)	58 (8.9)	51 (10.9)	56 (10.4)	51 (8.2)	65 (18.8)
SGRQ-c change, mean score difference (SE or 95%CI)							
FF/UMEC/VI vs FF/VI	−1.8 (−2.4, −1.1)	−1.5 (0.7)	−1.9 (0.4)	−2.0 (0.5)	−1.7 (0.5)	−2.2 (0.4)	−0.6 (0.7)
FF/UMEC/VI vs UMEC/VI	−1.8 (−2.6, −1.0)	−0.3 (0.9)	−2.2 (0.5)	−1.4 (0.6)	−2.1 (0.6)	−1.5 (0.5)	−2.7 (0.9)
Moderate exacerbation reduction, relative risk (SE or 95%CI)							
FF/UMEC/VI vs FF/VI	0.8 (0.8, 0.9)	0.8 (0.1)	0.9 (0.0)	0.8 (0.0)	0.9 (0.0)	0.8 (0.0)	1.0 (0.1)
FF/UMEC/VI vs UMEC/VI	0.8 (0.7, 0.8)	0.8 (0.1)	0.8 (0.0)	0.9 (0.1)	0.7 (0.0)	0.8 (0.0)	0.6 (0.1)
Severe exacerbation reduction, relative risk (SE or 95%CI)							
FF/UMEC/VI vs FF/VI	0.9 (0.8, 1.0)	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)	0.8 (0.1)	0.8 (0.1)	1.1 (0.2)
FF/UMEC/VI vs UMEC/VI	0.7 (0.6, 0.8)	1.0 (0.2)	0.6 (0.1)	0.9 (0.1)	0.5 (0.1)	0.8 (0.1)	0.4 (0.1)

Source: IMPACT Clinical Trial Supplementary Materials; EOS subgroup data from CTT116855 Japan Study Pop outputs 16Dec2019 Table #101.203.
Note: mMRC score ≥2 assumed the same as CAT ≥21.

Base case and scenario settings

- All scenarios were conducted from the perspective of the UK NHS and made the following assumptions:
  - The IMPACT trial population is representative of the UK COPD population likely to receive FF/UMEC/VI, FF/VI or UMEC/VI
  - Treatment effect is considered ongoing (persistent) at a constant rate over time for all patients on FF/UMEC/VI, FF/VI or UMEC/VI
- In the base case, a discount rate of 3.5% for costs and QALYs was applied, and treatment discontinuation was assumed to be 18.3% for FF/UMEC/VI, 25.2% for FF/VI and 27.3% for UMEC/VI in the first year. For subsequent years, discontinuation rates were assumed to be the same as first year
- Assumptions for individual scenario analyses included:
  - Discount rate at 0% or 5%
  - Treatment discontinuation at 18.3% for FF/UMEC/VI, 25.2% for FF/VI, and 27.3% for UMEC/VI in the first year only, or 0% for all treatments in first and subsequent years

Model outputs

- The model outputs included:
  - Clinical outcomes, number of exacerbations over time (moderate and severe) and exacerbations per patient per year
  - Final health outcomes (costs [total, drug, non-drug, reported separately]; proportion of patients surviving; LYs and QALYs)

Results

Summary of cost-effectiveness analyses

- Over a life-time horizon, at a willingness-to-pay threshold of £20 000 per QALY, FF/UMEC/VI was a cost-effective treatment option vs comparators across all EOS subgroups **(Table 2)**
- Total accumulated costs were higher for FF/UMEC/VI compared to FF/VI, while they fluctuated compared to UMEC/VI
  - Non-drug costs were lower for FF/UMEC/VI, regardless of subgroup
- The additional LYs and QALYs provided by FF/UMEC/VI were largely due to its favourable treatment effects for FEV_1, St George's Respiratory Questionnaire score and exacerbations
- These results were consistent across all scenario analyses, including: time horizon (5 years and 10 years); discount rate (0% and 5%); discontinuation (in first year only and excluded); duration of treatment effect (3 years); treatment effect for subsequent treatment (same as FF/UMEC/VI); patient productivity costs (included)

Conclusion

- FF/UMEC/VI was a cost-effective treatment option vs FF/VI and UMEC/VI across all baseline EOS count sub-groups
  - Compared to UMEC/VI, cost effectiveness of FF/UMEC/VI increased with baseline EOS count
- Although results of this analysis were consistent across most scenarios, the modelling approach relies on assumptions, which may limit the validity of the results
- Nevertheless, FF/UMEC/VI is expected to be a cost-effective treatment option for patients with COPD in the UK, irrespective of baseline blood EOS count

Table 2: Cost-effectiveness analyses of FF/UMEC/VI vs FF/VI and UMEC/VI by baseline blood EOS count

	Baseline EOS cut-points	Sample size (FF/UMEC/VI vs FF/VI)	Incremental LYs, undiscounted (95% CI)	Incremental QALYs (95% CI)	Incremental costs, £ (95% CI)	ICER/QALY, £ (95% CI)
FF/UMEC/VI vs FF/VI	ITT	4151 vs 4134	0.139 (0.070, 0.209)	0.124 (0.085, 0.165)	611 (307, 934)	4,925 (2,464, 8,171)
	<100 /µl	1065 vs 1014	0.130 (0.056, 0.207)	0.109 (0.050, 0.170)	685 (123, 1336)	6,284 (1,063, 18,319)
	≥100 /µl	3078 vs 3111	0.142 (0.071, 0.210)	0.129 (0.086, 0.172)	576 (241, 921)	4,471 (1,902, 8,176)
	<150 /µl	1844 vs 1769	0.154 (0.071, 0.239)	0.137 (0.085, 0.190)	796 (300, 1361)	5,820 (2,123, 12,190)
	≥150 /µl	2299 vs 2356	0.128 (0.064, 0.194)	0.116 (0.073, 0.162)	478 (132, 836)	4,117 (1,167, 8,531)
	<300 /µl	3280 vs 3212	0.152 (0.078, 0.226)	0.144 (0.099, 0.187)	484 (179, 809)	3,365 (1,288, 5,987)
	≥300 /µl	863 vs 913	0.095 (0.010, 0.174)	0.061 (−0.007, 0.127)	1,041 (62, 2086)	16,987 (dominant, 148,837)
FF/UMEC/VI vs UMEC/VI	ITT	4151 vs 2070	0.118 (0.047, 0.187)	0.116 (0.073, 0.159)	−370 (−635, −136)	Dominant (dominant, dominant)
	<100 /µl	1065 vs 512	0.079 (0.007, 0.156)	0.044 (−0.028, 0.114)	389 (−339, 1333)	8,789 (dominant, 109,796)
	≥100 /µl	3078 vs 1553	0.127 (0.050, 0.205)	0.134 (0.084, 0.184)	−523 (−796, −274)	Dominant (dominant, dominant)
	<150 /µl	1844 vs 869	0.085 (0.028, 0.146)	0.086 (0.032, 0.139)	269 (−287, 930)	3,134 (dominant, 17,577)
	≥150 /µl	2299 vs 1196	0.134 (0.048, 0.223)	0.134 (0.081, 0.190)	−650 (−926, −401)	Dominant (dominant, dominant)
	<300 /µl	3280 vs 1597	0.095 (0.043, 0.153)	0.094 (0.054, 0.136)	57 (−292, 425)	610 (dominant, 5,463)
	≥300 /µl	863 vs 468	0.167 (0.055, 0.282)	0.170 (0.086, 0.252)	−1045 (−1406, −764)	Dominant (dominant, dominant)

Note: A negative ICER value indicates that FF/UMEC/VI has lower costs and higher effectiveness, and is considered the dominant treatment option in these instances.

EOS subgroup analyses

- For FF/UME/VI vs UMEC/VI, costs were lower and incremental QALYs were higher for subgroups with higher baseline EOS count
- For FF/UME/VI vs FF/VI, costs were lower for subgroups with a higher baseline EOS count, while QALYs did not appear to show consistent variation with EOS count
- The ICER showed higher cost-effectiveness for FF/UMEC/VI compared to UMEC/VI in subgroups with a higher baseline EOS count but not compared to FF/VI **(Table 2)**
- The positive relationship between increasing baseline EOS count and cost-effectiveness for FF/UMEC/VI compared to UMEC/VI, but not compared to FF/VI, was also consistent across most scenarios

Abbreviations

BMI, body mass index; CAT, COPD assessment test; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; EOS, eosinophil; FEV_1, forced expiratory volume in 1 second; FF, fluticasone furoate; ICER, incremental cost-effectiveness ratio; ITT, intent-to-treat; LY, life year; mMRC, Modified Medical Research Council dyspnoea scale; NHS, national health service; QALY; quality-adjusted life year; SE, standard error; SGRQ-c, George's respiratory questionnaire for COPD patients; UMEC, umeclidinium; VI, vilanterol

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Acknowledgements

The Authors would like to thank Nancy Risebrough for her involvement in the study. Editorial support (in the form of writing assistance, including preparation of the draft poster under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing and referencing) was provided by Shannon Guild of OPEN Health Communications, and was funded by GSK

Disclosures

This study was funded by GSK (study ID: 206973). On behalf of all authors, an audio recording of this poster was prepared by Afisi S. Ismaila, who did not receive any payment for this recording. The authors declare the following real or perceived conflicts of interest during the last three years in relation to this presentation: ASI, AM, SGN and CC are employees of, and hold stock/shares in, GSK. ASI is also a part-time, unpaid professor at McMaster University. DS, RK and PD are employed by ICON plc., which received funding from GSK to conduct this study

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