Clinical and Economic Benefits of Prompt Initiation of Single-Inhaler Triple Therapy in COPD Patients in England Following an Exacerbation

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Background

Triple therapy with an inhaled corticosteroid, a long-acting muscarinic antagonist and a long-acting β_2-agonist is recommended for patients with chronic obstructive pulmonary disease (COPD) who remain symptomatic, or experience recurrent exacerbations, despite dual therapy[1]

Traditionally, triple therapy required multiple inhalers; however, the use of multiple inhalers has been shown to negatively affect treatment adherence and persistence among patients with COPD[2,3]

More recently, single-inhaler triple therapies (SITTs) have been developed to facilitate greater treatment adherence and persistence to therapy

There is limited real-world evidence to inform the optimum timing of SITT initiation following a COPD exacerbation

Aims

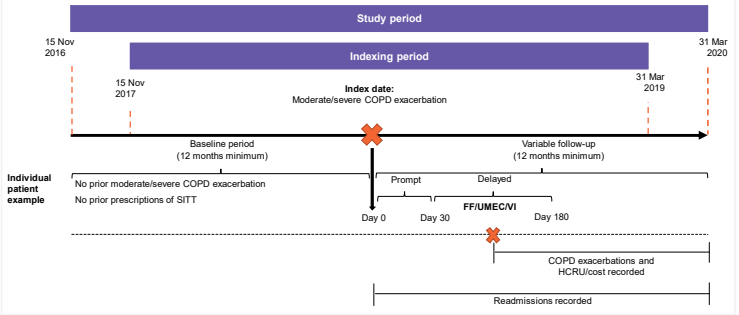
The aim of this study was to investigate the clinical and economic impact of prompt versus delayed initiation of SITT with fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) following a moderate or severe COPD exacerbation

Methods

This was a retrospective cohort study of English patients with COPD using primary care electronic health records (Clinical Practice Research Datalink Aurum) and linked secondary care data (Hospital Episode Statistics Admitted Patient Care database and Accident and Emergency datasets)

The index date was the first and/or earliest date of COPD exacerbation (moderate or severe) between 15 November 2017 (approval date of FF/UMEC/VI in Europe) and 31 March 2019 (to avoid the COVID-19 pandemic) (**Figure 1**)

Figure 1. Study design



COPD, chronic obstructive pulmonary disease; FF/UMEC/VI, furoate/umeclidinium/vilanterol; HCRU, healthcare resource utilisation; SITT, single-inhaler triple therapy

The baseline period was defined as the 12 months prior to index; the minimum follow-up period (from, and including, the index date) was 12 months

Two mutually exclusive cohorts were defined:

- Prompt initiators: FF/UMEC/VI therapy was initiated within 0–30 days of the index date
- Delayed initiators: FF/UMEC/VI therapy was initiated within 31–180 days of the index date

Inverse probability of treatment weighting (IPTW) was used to adjust for measured confounders (baseline covariates e.g., demographic, clinical, treatment-related and HCRU-related factors) between cohorts

Regression modelling was used when time to FF/UMEC/VI initiation was used as a continuous metric rather than dichotomous. The same covariates were considered as per IPTW

Inclusion criteria	Exclusion criteria
A diagnosis of COPD at age ≥35 years	≥1 COPD exacerbation (moderate or severe) during baseline
≥1 moderate or severe COPD exacerbation on or after 15 November 2017	≥1 prescription for SITT (FF/UMEC/VI or BDP/FOR/GLY) prior to the index date
Most recent smoking status prior to index date of 'current' or 'former' smoker	≥1 prescription for BDP/FOR/GLY between the index date and FF/UMEC/VI initiation
≥1 prescription for FF/UMEC/VI on or within 180 days of the index date	≥1 diagnostic code for any medical condition incompatible with a COPD diagnosis at any point in medical history
Continually registered with a primary care practice for ≥12 months prior to index (baseline) and 12 months following index, and have records linked to HES	

BDP/FOR/GLY, beclomethasone dipropionate/formoterol fumarate/glycopyrronium bromide; COPD, chronic obstructive pulmonary disease; FF/UMEC/VI, furoate/umeclidinium/vilanterol; HES, Hospital Episode Statistics; SITT, single-inhaler triple therapy

Hospital readmissions, and subsequent moderate/severe exacerbations and medical costs, were compared between prompt and delayed initiators following index and FF/UMEC/VI initiation, respectively

The associated impact of prompt initiation (per day) was estimated using regression models adjusted for potential confounders

Results

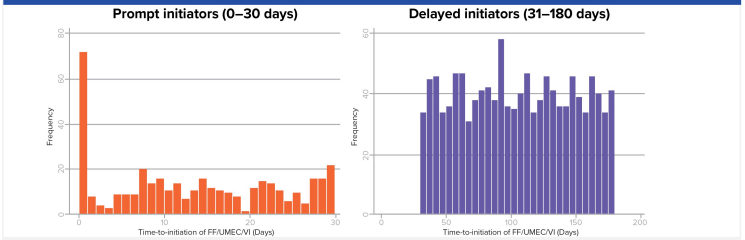
In total, 1599 patients were included (**Table 1**); 393 patients (24.6%) had prompt FF/UMEC/VI initiation (within 30 days of the index COPD exacerbation) (**Figure 2**)

Table 1. Baseline demographics

	Total (N=1599)	Prompt (0–30 days) (n=393)	Delayed (31–180 days) (n=1206)
Age at index, years, mean (SD)	69.8 (10.3)	69.5 (9.8)	69.9 (10.5)
Male, n (%)	847 (53.0)	218 (55.5)	629 (52.2)
Smoking status, n (%)			
Current smoker	811 (50.7)	216 (55.0)	595 (49.3)
Current asthma, n (%)	426 (26.6)	90 (22.9)	336 (27.9)
MRC group, n (%)			
<3	561 (35.1)	136 (34.6)	425 (35.2)
≥3	879 (55.0)	230 (58.5)	649 (53.8)
Unknown	159 (9.9)	27 (6.9)	132 (10.9)
FEV_1% predicted	n=1289	n=326	n=963
Mean (SD)	55.7 (19.5)	53.5 (18.7)	56.4 (19.7)

FEV_1, forced expiratory volume in 1 second; MRC, Medical Research Council; SD, standard deviation

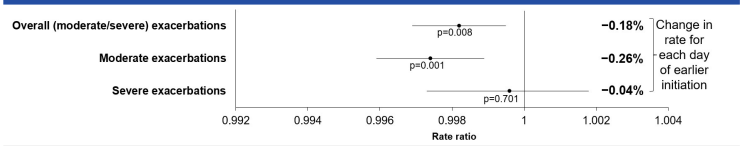
Figure 2. Time to initiation of FF/UMEC/VI for prompt and delayed initiators



FF/UMEC/VI, furoate/umeclidinium/vilanterol

For each day of earlier initiation of FF/UMEC/VI, the rate of subsequent moderate/severe exacerbations and moderate exacerbations were significantly lower, and the rate of subsequent severe exacerbations was numerically lower (**Figure 3**)

Figure 3. Rate of subsequent COPD exacerbations



RRs are for each day of earlier initiation, and they are multiplicative; therefore, initiation 7 days earlier would result in an RR of 0.9982^7=0.9875 (1.25% reduction in rate) for overall exacerbations. COPD, chronic obstructive pulmonary disease; RR, rate ratio

For each day of earlier initiation of FF/UMEC/VI, the odds of all-cause hospital readmission were significantly lower, and the odds of COPD-related hospital readmission were numerically lower for 30-, 60- and 90-day readmissions (**Table 2**)

Table 2. Risk of hospital readmission

	Change in odds for each day of earlier initiation	OR*	95% CI	p-value
30-day readmission				
All-cause	−0.60%	0.9940	0.9886, 0.9994	0.029
COPD-related	−0.36%	0.9964	0.9911, 1.0017	0.186
60-day readmission				
All-cause	−0.57%	0.9943	0.9894, 0.9992	0.024
COPD-related	−0.26%	0.9974	0.9924, 1.0025	0.322
90-day readmission				
All-cause	−0.49%	0.9951	0.9904, 0.9998	0.039
COPD-related	−0.32%	0.9968	0.9921, 1.0016	0.197

*ORs are for each day of earlier initiation, and they are multiplicative; therefore, initiation 7 days earlier would result in an OR of 0.9940^7=0.9587 (4.13% reduction in rate) for 30-day all-cause readmissions. CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio

Total all-cause medical costs were numerically higher for each day of earlier initiation of FF/UMEC/VI. Total COPD-related medical costs were significantly lower for each day of earlier initiation of FF/UMEC/VI (**Table 3**)

Table 3. Medical costs

Medical costs	Change in cost for each day of earlier initiation	Exponentiated coefficient*	95% CI	p-value
All-cause				
Prescription medications	**−0.13%**	**0.9987**	**0.9978, 0.9997**	**0.008**
GP/nurse consultations	−0.05%	0.9995	0.9988, 1.0001	0.088
Inpatient stays	+0.10%	1.0010	0.9990, 1.0030	0.331
A&E attendances	+0.10%	1.0010	0.9991, 1.0030	0.302
Total costs	+0.04%	1.0004	0.9991, 1.0016	0.589
COPD-related				
Prescription medications	**−0.05%**	**0.9995**	**0.9992, 0.9998**	**0.002**
GP/nurse consultations	**−0.09%**	**0.9991**	**0.9984, 0.9997**	**0.006**
Inpatient stays	+0.24%	1.0024	0.9991, 1.0058	0.155
A&E attendances	−0.04%	0.9996	0.9957, 1.0036	0.857
Total costs	**−0.05%**	**0.9995**	**0.9992, 0.9999**	**0.005**

*Estimates are for each day of earlier initiation, and they are multiplicative; therefore, initiation 7 days earlier would result in an exponentiated coefficient of 0.9987^7=0.9909 (0.91% reduction) in all-cause prescription medication costs. A&E, accident and emergency; CI, confidence interval; COPD, chronic obstructive pulmonary disease; GP, general practitioner

Limitations

Survivorship bias; patients who died within 12 months of the index exacerbation have been excluded

Only medications prescribed in the primary care setting are captured; medications initiated in hospital and continued by a general practitioner may have led to the incorrect classification of 'delayed initiators' for some patients

Conclusions

Prompt initiation of FF/UMEC/VI following an exacerbation of COPD was associated with fewer subsequent exacerbations and hospital readmissions, and lower costs relative to delayed initiation

Benefits were seen with each day of earlier initiation, suggesting that the optimal timing for initiation of FF/UMEC/VI may be shortly after index exacerbation

Disclosures

The authors declare the following real or perceived conflicts of interest during the last three years in relation to this presentation:
- ASI, AC, RS, CC and KJR are employees of GSK and/or hold stocks/shares in GSK. ASI is also a part-time member of the McMaster University faculty
- RPW, VLB (at time of study), LJC and OKM are employees of Adelphi Real World; Adelphi Real World received funds from GSK to conduct the study although not for poster development

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