Adherence to single and multiple inhaled triple therapies in patients with COPD in Germany, considering different definitions



PCR255

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Introduction



Adherence to therapy is critical for achieving optimal clinical outcomes among patients with COPD^{1,2}

Evidence shows that adherence to MITT is low in real-world settings;^{3,4} SITT has the potential to improve adherence by reducing the number of inhalers required^{3,5}



Adherence can be assessed via different measures, with factors such as stockpiling and periods of hospitalization potentially affecting the outcome⁶

There is limited evidence on the impact of SITT on

Results

- In total, 5710 patients were included. Of these, 4079 (71%) initiated MITT and 1631 (29%) initiated SITT (FF/UMEC/VI, 12%; FOR/BDP/GLY, 17%)
- The mean age was 66 years across all cohorts (Table 2)

Table 2: Unadjusted baseline characteristics – overall population

Characteristic	MITT (n=4079)	SITT (n=1631)	FF/UMEC/VI (n=675)	FOR/BDP/GLY (n=956)
Mean age, years	66	66	66	66
Male, %	55.1	60.2	60.6	59.8
Smoker, %	42.9	45.6	46.5	44.9
FEV ₁ <50%*, %	7.6	7.2	6.1	8.0
Mean CCI score	2.3	2.2	2.2	2.2
Arthritis, %	38.0	37.7	36.3	38.7
Anxiety, %	31.3	30.4	27.7	32.3
Depression, %	28.7	25.2	23.3	26.6
Asthma, %	23.7	13.2	12.9	13.4
GERD, %	19.9	18.5	19.4	17.9

Conclusions

- The observed increase in adherence for SITT versus MITT initiators was consistent for all analyses and lasted up to 18 months following treatment initiation
- FF/UMEC/VI users appeared to have the highest adherence for each definition of adherence and at each time point
- Although considering different definitions of adherence yielded varying absolute differences, the relative differences between definitions remained the same

treatment adherence among patients with COPD in Germany



The objective of this study was to describe and compare medication adherence among patients with COPD in Germany, who initiated MITT or SITT

Methods

- A retrospective cohort study of patients with COPD who initiated triple therapy (MITT or SITT [FF/UMEC/VI or FOR/BDP/GLY]), using the WIG2 benchmark database
- The index date was defined as the first/earliest date of triple therapy initiation in the indexing period (Figure 1)
- For MITT users, this was defined as the first date of overlapping supply of all three components of triple therapy (a minimum of 30 days overlap was required to define MITT use)

Figure 1: Study design



*FEV₁ <50% was captured via ICD-10-GM diagnosis codes, not by clinical measures.

- Adherence was higher for SITT initiators versus MITT initiators at all time points and for all definitions of adherence examined (Figure 2)
- All analyses yielded consistent results; the highest proportion of adherent patients was observed for the adherence definition 1b (adherence only reported during periods of continuous therapy) at 6-months post index: 59% of patients on SITT; 64% of patients on FF/UMEC/VI; 57% of patients on FOR/BDP/GLY (Figures 2–4, respectively)
- Similar trends were observed at 12 and 18 months (Figures 2–4)
- Taking hospitalization into account during assessment of adherence appeared to make little difference, evidenced by the similar results between definitions 2 and 3
- Overall, these results suggest that a reduction in the number of inhalers required may improve adherence, irrespective of the definition used
- These data support GOLD guideline recommendations for the use of SITT over MITT

Figure 2: Proportion of patients adherent to therapy across different definitions of adherence (M, 1a, 1b, 2, and 3) at 6-, 12-, and 18-months post index, IPTW weighted: MITT* vs SITT



period	minimum follow-up period required	months, only patients with that length of follow-up were included		
Inclusion criteria		Exclusion criteria		
Aged ≥35 years at index				
≥1 inpatient and/or ≥2 confirmed outpatient diagnoses of COPD at any time in the patient's medical history		≥1 diagnostic code for any medical condition incompatible with a COPD diagnosis at any time in the patient's medical history that can interfere with the clinical diagnosis of COPD or substantially change the		
Outpatient prescription for triple therapy (MITT or SITT) during the inclusion period				
Continuously insured for a minimum of 2 years leading up to the index date				
No previous pre triple the	scriptions for erapy	natural history of the disease		

- Adherence (as measured by PDC [number of days covered/number of days in the period]) was assessed at 6-, 12-, and 18-months post index, among patients with sufficient follow-up
- Different definitions of adherence were analyzed to assess the influence of different scenarios on PDC (**Table 1**). Patients were categorized as adherent (PDC \geq 80%) or non-adherent (PDC <80%)
- IPTW using PS-based methodology was used to adjust for measured confounders between the cohorts. Covariates considered for inclusion in the PS model included demographics, clinical characteristics, comorbidities, and prior therapy. An SMD <0.1 was considered a negligible imbalance between the cohorts

Table 1: Different definitions of adherence considered

Definition	Explanation
Main approach (M)	All patients. No stockpiling or periods of hospitalization considered

6 months 12 months 18 months Figure 3: Proportion of patients adherent to therapy across different definitions of adherence (M, 1a, 1b, 2, and 3) at 6-, 12-, and 18-months post index, IPTW weighted: MITT* vs FF/UMEC/VI



Figure 4: Proportion of patients adherent to therapy across different definitions of adherence (M, 1a, 1b, 2, and 3) at 6-, 12-, and 18-months post index, IPTW weighted: MITT* vs FOR/BDP/GLY



1a	Patients with ≥1 follow-up prescription for the index triple therapy within 2 months of initiation
1b	Patients with periods of continuous therapy (e.g. no discontinuation* or treatment switches)
2	Patients with stockpiled therapy (i.e. treatment supply could be allocated to a later point in the observation period)
3	Patients with stockpiled therapy and periods of hospitalization were considered covered

*Medication discontinuation was defined as a gap of >30 days between the end of a SITT prescription and the following refill, or a gap of >30 days between prescriptions in any of the three MITT components.

*Values for MITT may vary slightly between comparisons due to weighting.

Limitations

- The definition of MITT may misclassify patients who are switching therapies as it is impossible to know with certainty whether all prescribed agents were taken simultaneously
- Pharmacy claims records do not contain number of intakes per day, so the usage was according to the approved product label

• Some of the therapies included in this analysis are also used in patients with asthma diagnoses. In cases where agents are prescribed to patients with COPD and asthma, it may be impossible to disentangle COPD treatment from systematic treatment of uncontrolled asthma

Abbreviations

CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; FEV,, forced expiratory volume in 1 second; FF/UMEC/VI, fluticasone furoate/umeclidinium/vilanterol; FOR/BDP/GLY, formoterol/ beclomethasone/glycopyrronium; GERD, gastroesophageal reflux disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICD-10-GM, International Classification of Diseases, 10th Revision, German modification; IPTW, inverse probability of treatment weighting; MITT, multiple-inhaler triple therapy; PDC, proportion of days covered; PS, propensity score; SITT, single-inhaler triple therapy; SMD, standardized mean difference.

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