Demographic and Clinical Characteristics of Patients Experiencing On-Treatment Exacerbations, On-Treatment Death or Premature Study Treatment Withdrawal: The IMPACT Trial

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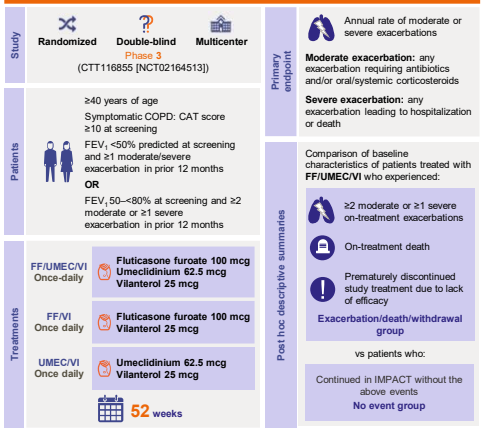
Introduction

- In the InforMing the PAthway of COPD Treatment (IMPACT) trial, once-daily single-inhaler triple therapy with the inhaled corticosteroid (ICS), long-acting muscarinic antagonist (LAMA) and long-acting β_2-agonist (LABA) combination of fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) resulted in a significantly lower annual rate of moderate/severe exacerbations than dual therapy with FF/VI (an ICS/LABA) or UMEC/VI (a LAMA/LABA) in patients with symptomatic COPD and a history of exacerbations.[1]
- In addition, FF/UMEC/VI was associated with a significantly reduced risk of all-cause mortality compared with UMEC/VI.[2]
- Patients who have experienced exacerbations in the past 12 months, have more severe lung function impairment or have comorbidities, such as cardiovascular disease, have been previously shown to have an increased risk of exacerbations or mortality, and worse clinical outcomes compared with patients without these risk factors.[3-5]
- These post hoc descriptive summaries assessed whether there were any differences in baseline characteristics between patients treated with FF/UMEC/VI in the IMPACT trial who experienced on-treatment exacerbation, on-treatment death or prematurely discontinued study treatment due to a lack of efficacy compared with those who did not experience these events over the duration of the study.

Methods



CAT, COPD Assessment Test; FEV_1, forced expiratory volume in 1 second.

Results

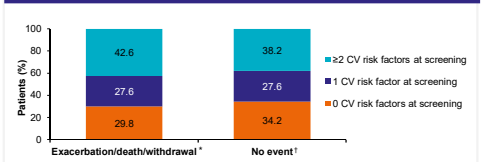
- Of 10,355 patients included in the intent-to-treat population, 4151 received FF/UMEC/VI (Exacerbation/death/withdrawal group: n=1188; No event group: n=2963). Age, sex, race, body mass index, blood eosinophil level, and smoking status at screening were similar across both groups (**Table 1**). In total, 89% of patients completed the study and 82% completed on-treatment on FF/UMEC/VI.
- More patients in the Exacerbation/death/withdrawal group were receiving ICS+LAMA+ LABA at screening than in the No event group. Baseline SGRQ total score and CAT score at screening was lower in the No event group compared with the Exacerbation/death/withdrawal group (**Table 1**).
- A total of 834 (70%) patients had at least 1 CV risk factor in the Exacerbation/death/withdrawal group compared with 1952 (66%) patients in the No event group (**Figure 1**).
- A greater proportion of patients in the Exacerbation/death/withdrawal group presented with more severe lung function impairment than in the No event group (**Figure 2** and **Table 2**).
  - Percent reversibility to albuterol and the proportion of patients reversible to albuterol was similar between both groups (**Table 2**).
- In the 12 months prior to screening, a higher proportion of patients in the Exacerbation/death/withdrawal versus No event group experienced ≥3 moderate or severe exacerbations (**Figure 3**).
  - A higher proportion of patients in the Exacerbation/death/withdrawal group versus the No event group had ≥2 COPD exacerbations treated with either systemic/oral corticosteroids (41 vs 35%) or treated with antibiotics (43 vs 39%) in the 12 months prior to screening.

Table 1. Baseline patient demographics

	Exacerbation/death/withdrawal (n=1188)	No event (n=2963)
Age, years, mean (SD)	65.4 (8.1)	65.3 (8.3)
Male, n (%)	759 (64)	2007 (68)
BMI, kg/m², mean (SD)*	26.6 (6.6)	26.6 (6.1)
Smoker at screening, n (%)		
Current	419 (35)	1017 (34)
Former	769 (65)	1946 (66)
Blood eosinophil level (10^9/L), mean (SD)†	0.23 (0.2)	0.22 (0.2)
CAT score at screening, mean (SD)‡	21.1 (6.3)	19.6 (6.0)
SGRQ score, mean (SD)#	55.6 (15.9)	48.9 (16.8)
Medication at screening, n (%)		
ICS+LAMA+LABA	615 (52)	1057 (36)
ICS+LABA	309 (26)	1045 (35)
LAMA+LABA	109 (9)	280 (9)
LAMA	60 (5)	244 (8)
Other¶	95 (8)	337 (11)
Current medical conditions, n (%)		
Cardiac disorder	205 (17)	451 (15)
Vascular disorder	596 (50)	1491 (50)
Metabolism and nutrition disorder	507 (43)	1193 (40)
Infection and infestation	11 (<1)	14 (<1)

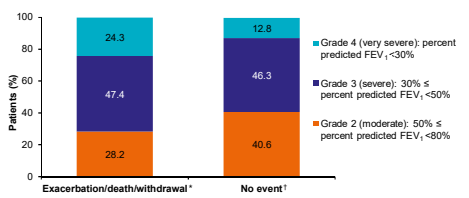
*Exacerbation/death/withdrawal group, n=1187; No event group, n=2961; †Exacerbation/death/withdrawal group, n=1187; No event group, n=2956. ‡Exacerbation/death/withdrawal group, n=1187; No event group n=2955. #Exacerbation/death/withdrawal group, n=1174; No event group n=2934. ¶Includes ICS+LAMA therapy, ICS monotherapy; LABA monotherapy or no ICS, LABA, LAMA. BMI, body mass index.

Figure 1. Number of CV risk factors at screening in patients randomized to FF/UMEC/VI by on-treatment exacerbation/death/withdrawal status



*n=1188 (0 CV risk factors at screening, n=354; 1 CV risk factor at screening, n=328; ≥2 CV risk factors at screening, n=506); †n=2963 (0 CV risk factors at screening, n=1011; 1 CV risk factor at screening, n=819; ≥2 CV risk factors at screening, n=1133). CV risk factors include past or current medical conditions recorded at screening. Risk factors included angina pectoris, coronary artery disease, myocardial infarction, arrhythmia, congestive heart failure, hypertension, cerebrovascular accident, carotid or aorto-femoral vascular disease, hypercholesterolemia and diabetes mellitus.

Figure 2. GOLD lung function grade at screening in patients randomized to FF/UMEC/VI by on-treatment exacerbation/death/withdrawal status



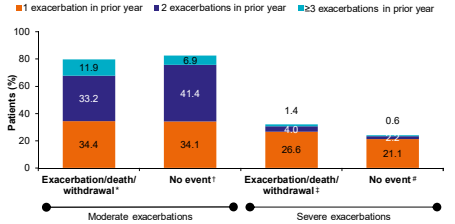
*n=1187 (GOLD grade 1, n=1 [<1% data not shown]; GOLD grade 2, n=335; GOLD grade 3, n=563; GOLD grade 4, n=288); †n=2958 (GOLD grade 1, n=9 [<1% data not shown]; GOLD grade 2, n=1200; GOLD grade 3, n=1371; GOLD grade 4, n=378). GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Table 2. Lung function at screening in patients randomized to FF/UMEC/VI, by on-treatment exacerbation/death/withdrawal status

	Exacerbation/death/withdrawal (n=1187)	No event (n=2958)
Post-bronchodilator FEV_1, L	1.14 (0.46)	1.33 (0.49)
Post-bronchodilator predicted FEV_1, %	41.7 (15.0)	47.3 (14.7)
Post-bronchodilator FEV_1/FVC ratio	0.44 (0.12)	0.48 (0.12)
Reversibility to albuterol, %	11.0 (12.4)†	10.1 (12.4)
Reversible to albuterol,* n (%)	192 (16)†	542 (18)

All data are mean (SD) unless otherwise stated. *Reversible is an increase in FEV_1 of ≥12% and ≥200 mL following administration of albuterol; †n=1186.

Figure 3. Summary of COPD exacerbation history at screening in patients randomized to FF/UMEC/VI, by on-treatment exacerbation/death/withdrawal status



*n=1188 (1 exacerbation in prior year, n=409; 2 exacerbations in prior year, n=395; ≥3 exacerbations in prior year, n=141); †n=2963 (1 exacerbation in prior year, n=1009; 2 exacerbations in prior year, n=1227; ≥3 exacerbations in prior year, n=204); ‡n=1188 (1 exacerbation in prior year, n=316; 2 exacerbations in prior year, n=48; ≥3 exacerbations in prior year, n=17); #n=2963 (1 exacerbation in prior year, n=624; 2 exacerbations in prior year, n=64; ≥3 exacerbations in prior year, n=18).

Conclusions

- In IMPACT, patients receiving FF/UMEC/VI who had on-treatment exacerbations, died or prematurely withdrew study treatment were more likely to have more severe airflow limitation at screening, in terms of GOLD lung function grade, lung function impairment and exacerbation history, and more CV comorbidities than those who continued in the study without these events.
- Severe lung function impairment, a history of >3 exacerbations in prior year or ≥2 CV risk factors were characteristics observed more frequently in patients experiencing adverse outcomes while on treatment. These data suggest that patients with these characteristics may require additional attention to ensure early treatment optimization and exclude other factors that contribute to their respiratory complaints.

Disclosures

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