Risk of Death and Chronic Obstructive Pulmonary Disease (COPD) Hospitalization with Fluticasone Furoate-Containing Therapy: Post Hoc Subgroup Analysis From the SUMMIT Trial in Patients with COPD and a History of Exacerbation

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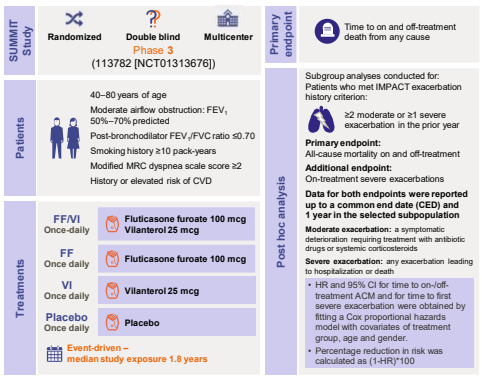
Introduction

- The event-driven SUMMIT trial (NCT01313676) investigated the efficacy of fluticasone furoate (FF), an inhaled corticosteroid (ICS) and vilanterol (VI), a long-acting β_2-agonist (LABA), both as monotherapy and in combination, in patients with COPD and with moderate airflow limitation and heightened cardiovascular (CV) risk. No significant difference in all-cause mortality (ACM) was seen with FF/VI, FF or VI treatment compared with placebo in the overall ITT population.[1]
- However, in the 1-year IMPACT trial (NCT02164513), triple therapy with FF/umeclidinium (UMEC)/VI significantly reduced the risk of on-/off-treatment ACM in patients with a history of exacerbations compared with UMEC/VI.[2,3]
- A history of moderate or severe exacerbations was not an inclusion criterion in the SUMMIT trial,[1] whereas in the IMPACT trial patients with moderate airflow limitation were required to have an exacerbation history of ≥2 moderate or ≥1 severe exacerbation in the prior year.[2] We hypothesized that FF-based treatments would have had a beneficial effect on ACM in those SUMMIT patients with a history of exacerbations.
- This post hoc analysis tested this hypothesis using the ACM and severe exacerbations data from patients enrolled in SUMMIT who met the exacerbation inclusion criteria of IMPACT.

Methods



CVD included coronary artery disease, peripheral artery disease, previous stroke, previous myocardial infarction, and diabetes with target organ disease. CV risk was defined as the following: ≥60 years of age and receiving medication for >2 of hypercholesterolemia, hypertension, diabetes mellitus, and peripheral artery disease. On and off-treatment deaths are those which occur between study treatment start date and the minimum of the last known contact date, the CED and Day 365 inclusive. CED, common end date; CI, confidence interval; CVD, cardiovascular disease; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HR, hazard ratio; MRC, Medical Research Council.

Results

- The intent-to-treat population in SUMMIT comprised 16,485 patients. Of these, 3428 met the IMPACT trial exacerbation inclusion criterion and were included in this subgroup analysis. Baseline characteristics were similar across treatment arms (**Table 1**)
- Up to the CED:
  - Risk of on-/off-treatment death was significantly lower in all treatment arms versus placebo (**Figure 1** and **Figure 2**).
  - CV events were the most common primary cause of death, occurring in 22 (2.6%), 32 (3.7%), 31 (3.6%), and 40 (4.7%) patients in the FF, VI, FF/VI, and placebo treatment arms, respectively.
  - Compared with placebo, the risk of severe exacerbation was significantly less in the FF treatment arm, with numerical reductions seen for both the VI and FF/VI arms (**Figure 1**).
- In the analysis of data up to Day 365, no significant differences in on-/off-treatment ACM were seen between any treatment and placebo, although numerical reductions compared with placebo were seen in the FF and FF/VI treatment arms (**Figure 3** and **Figure 4**).
- Only FF was associated with a statistically significant reduction in severe exacerbation risk versus placebo up to Day 365, although numerical reductions were seen with FF/VI and VI (**Figure 3**).

Table 1. SUMMIT baseline patient characteristics in subanalysis population

	Placebo (N=857)	FF (N=840)	VI (N=866)	FF/VI (N=865)
Age, mean (SD) years	64.6 (8.0)	64.0 (8.40)	64.5 (8.2)	64.5 (8.4)
Male, n (%)	650 (76)	628 (75)	654 (76)	648 (75)
BMI, mean (SD) kg/m²	28.25 (5.98)	27.75 (6.07)	28.26 (6.12)	28.08 (5.74)
Former smoker, n (%)	484 (56)	456 (54)	443 (51)	463 (54)
% predicted post-bronchodilator FEV_1 at screening, mean (SD)	58.9 (6.09)	59.2 (6.00)	58.9 (6.09)	58.9 (6.03)
Moderate/severe exacerbations in prior year, n (%)				
1	237 (28)	241 (29)	236 (27)	270 (31)
≥2	620 (72)	599 (71)	630 (73)	595 (69)
Severe exacerbations in prior year, n (%)				
0	295 (34)	315 (38)	318 (37)	295 (34)
1	487 (57)	462 (55)	476 (55)	493 (57)
≥2	75 (9)	63 (8)	72 (8)	77 (9)
SGRQ total score, mean (SD)	52.9 (15.9)	52.9 (16.5)	53.2 (17.0)	52.1 (16.3)
CAT score, mean (SD)	21.1 (6.6)	20.9 (6.2)	21.0 (6.7)	20.3 (6.2)

BMI, body mass index; CAT, COPD Assessment Test; SD, standard deviation; SGRQ, St George's Respiratory Questionnaire

Figure 1. Risk of on-/off-treatment ACM and severe exacerbations with FF, VI and FF/VI vs placebo up to the CED

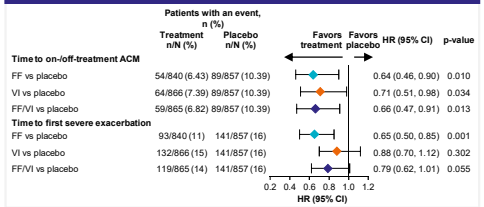


Figure 2. Kaplan–Meier plot of time to on-/off-treatment ACM up to the CED

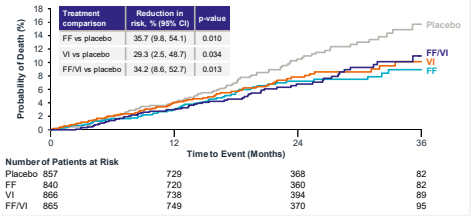


Figure 3. Risk of on-/off-treatment ACM and severe exacerbations with FF, VI and FF/VI vs placebo up to Day 365

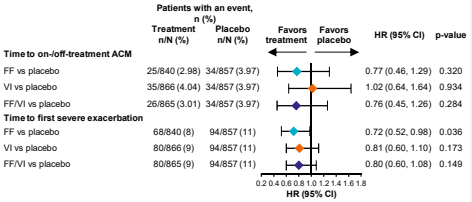
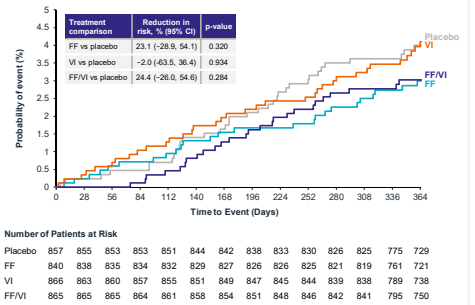


Figure 4. Kaplan–Meier plot of time to on-/off-treatment ACM up to Day 365



Conclusions

- This post hoc analysis showed that in a subpopulation of patients with moderate airflow limitation, heightened CV risk and a history of exacerbations in the SUMMIT study, risk of on-/off-treatment ACM was significantly lower in patients receiving FF, VI and FF/VI at CED and numerically reduced with FF and FF/VI at Day 365 compared with placebo.
- Risk of severe exacerbation was significantly lower in patients receiving FF monotherapy compared with placebo at CED and Day 365. Numerical reductions were seen in the VI and FF/VI arms at both timepoints
- In a subpopulation of patients with COPD at high risk of exacerbation, there appears to be a survival benefit with FF-containing therapies compared to placebo, in agreement with the results seen in the IMPACT trial.

Disclosures

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References

1. Vestbo J, et al. *Lancet*. 2016;387:1817–26
2. Lipson D, et al. *N Engl J Med*. 2018;3;378:1671–80.
3. Lipson, D et al. *Am J Resp Crit Care Med*. 2020;201:1508–16.

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