Time-dependent Risk of Cardiovascular Events Following an Exacerbation in Patients With COPD: Post Hoc Analysis From the IMPACT Trial

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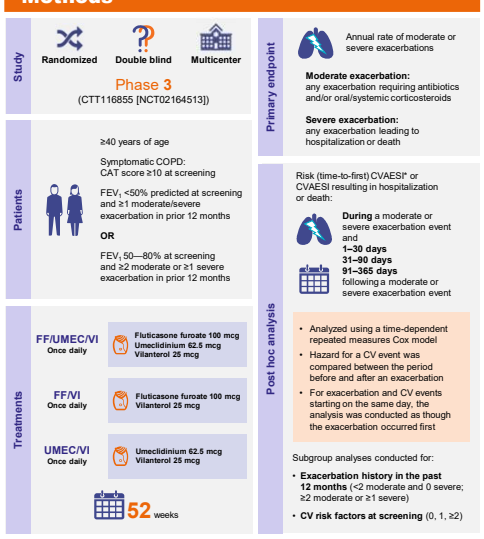
Introduction

- Patients with chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD), or risk factors for CVD, have been shown to be at increased risk of subsequent cardiovascular (CV) events following an exacerbation, particularly those patients requiring hospitalization for their exacerbation and within the first 30 days after an exacerbation.[1]
- The Phase 3 IMPACT trial assessed single-inhaler triple therapy with fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) versus FF/VI or UMEC/VI in patients with symptomatic COPD at risk of exacerbations and with varying degrees of CVD or CV risk.[2,3] This post hoc analysis evaluated the time-dependent risk of CV events following an exacerbation in patients with COPD who participated in the IMPACT trial.

Methods



*CVAESI included cardiac arrhythmia, cardiac failure, central nervous system hemorrhages, and cerebrovascular conditions, hypertension, and ischemic heart disease. CAT, COPD Assessment Test; CVAESI, cardiovascular adverse event of special interest; FEV_1, forced expiratory volume in 1 second.

Results

- A total of 10,355 patients were included in the intent-to-treat population (**Table 1**).
- Overall, the number of patients experiencing a CV event during or following an exacerbation was low (**Table 2**).

Table 1. Baseline characteristics[2,3]

	Total (N=10,355)
Age, mean (SD) years	65.3 (8.3)
Male, n (%)	6870 (66)
BMI, mean (SD) kg/m²	26.6 (6.1)
Former smokers, n (%)	6768 (65)
Exacerbation history in prior 12 months, n (%)	
<2 moderate and no severe exacerbations	3056 (30)
≥2 moderate or ≥1 severe exacerbation	7299 (70)
Postbronchodilator FEV_1 % predicted, mean (SD)	45.5 (14.8)
CAT score, mean (SD)	20.1 (6.1)
CV risk factors, n (%)*	
0	3343 (32)
1	2885 (28)
≥2	4127 (40)

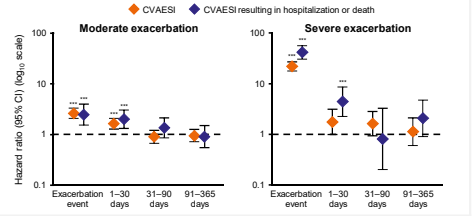
*As captured in the electronic case report form; CV risk factors included: angina pectoris; coronary artery disease; myocardial infarction; arrhythmia; congestive heart failure; hypertension; cerebrovascular accident; carotid or aorto-femoral vascular disease; diabetes mellitus; hypercholesterolemia. BMI, body mass index; SD, standard deviation.

Table 2. Number of patients experiencing first CV events during or following exacerbation events

Event	CVAESI		CVAESI resulting in hospitalization or death	
	Total n	Patients experiencing CV event, n (%)	Total n	Patients experiencing CV event, n (%)
Moderate exacerbations				
Exacerbation event	4207	80 (1.9)	4361	19 (0.4)
1–30 days post event	3874	74 (1.9)	4050	26 (0.6)
31–90 days post event	3410	49 (1.4)	3599	22 (0.6)
91–365 days post event	2548	61 (2.4)	2710	18 (0.7)
Severe exacerbations				
Exacerbation event	1099	124 (11.3)	1160	64 (5.5)
1–30 days post event	790	12 (1.5)	873	9 (1.0)
31–90 days post event	600	13 (2.2)	667	2 (0.3)
91–365 days post event	386	10 (2.6)	435	6 (1.4)

- A significantly increased risk of a CVAESI or CVAESI resulting in hospitalization or death was seen during a moderate or severe exacerbation event, which decreased over time thereafter (**Figure 1**).
  - The increase in the risk of a CVAESI or CVAESI resulting in hospitalization or death was higher during a severe exacerbation (hazard ratio: 21.84 and 41.29, respectively) than during a moderate exacerbation (hazard ratio: 2.63 and 2.46, respectively).

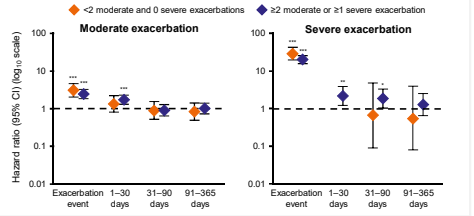
Figure 1. Risk of a first CVAESI or CVAESI resulting in hospitalization or death during or following a moderate or severe exacerbation event



***p<0.001 vs baseline period. CI, confidence interval.

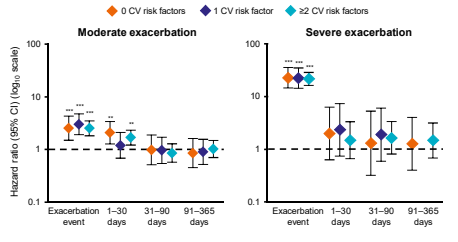
- A similar trend was seen in the subgroup analyses, with similar increases in risk of CVAESI regardless of patients exacerbation history (**Figure 2**) and CV risk factors at screening (**Figure 3**).

Figure 2. Risk of a first CVAESI during or following a moderate or severe exacerbation event by exacerbation history



*p<0.05; **p<0.01; ***p<0.001 vs baseline period. Note: no events were recorded within 1–30 days post severe exacerbation in the <2 moderate and 0 severe exacerbations subgroup.

Figure 3. Risk of a first CVAESI during or following a moderate or severe exacerbation event by CV risk factors at screening



*p<0.05; **p<0.01; ***p<0.001 vs baseline period. Note: no events were recorded within 91–365 days post severe exacerbation in the 1 CV risk factor subgroup.

Conclusions

- In IMPACT, while the overall number of patients experiencing CV events during or following an exacerbation was low, a significantly increased risk of CVAESI or CVAESI resulting in hospitalization or death was seen during a moderate or severe exacerbation, with the risk decreasing over time thereafter.
  - This increased risk was higher during a severe exacerbation compared with a moderate exacerbation regardless of CVAESI severity.
- A similar increase in risk was observed regardless of the presence of CV risk factors at screening or the patients' exacerbation history, with the risk increase following a similar pattern as in the overall analysis.
- This analysis confirms the increased risk of CVAESI during and in the first 30 days following an exacerbation seen in other studies, highlighting a need for exacerbation prevention and close patient monitoring following exacerbation events, irrespective of a patient's exacerbation history or CV risk factors.

Disclosures

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