In addition, FF/UMEC/VI was associated with a significantly reduced risk of all-cause mortality compared with UMEC/VI. 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.10,11

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.

### Results

- Of 10,355 patients included in the intent-to-treat population, 4,151 received FF/UMEC/VI (Exacerbation/death/withdrawal group: n=1,188; No event group: n=2,963). Age, sex, race, body mass index, blood eosinophil level, and smoking status at screening were similar across both groups (Table 1). In total, 88% 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 1,052 (69%) 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 ≥1 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 other systemic corticosteroids (41 vs 35%) or treated with antibiotics (43 vs 39%) in the 12 months prior to screening.

### 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.