Background

A Treatable trait approach has been proposed for the treatment of asthma, in which patients are characterized by the presence of pathophysiological disease characteristics and managed through an individualized treatment plan tailored to the patient’s specific characteristics.

The discovery of simple markers of type 2 airway inflammation (e.g., blood eosinophils and fractional exhaled nitric oxide [FeNO]) has opened new therapeutic approaches.

There is consistent evidence that type 2 airway inflammation is an independent predictor of the response to corticosteroids [1].

The Phase II CAPTAIN study evaluated the use of the inhaled corticosteroid/long-acting muscarinic antagonist/long-acting β–agonist (ICS/LABA). The study design is shown in Figure 1 (A and B).

Methods

Study population

234 participants were included in the ITT population, with 48 participants in each of the FF/100 mcg, FF/200 mcg, and FF 200 mcg/UMEC 31.25+62.5 mcg groups.

Pre-specified analyses

At the ITT population, FF/100 mcg resulted in a numerically lower rate of exacerbations versus FF/200 mcg, but the difference was not statistically significant.

In the ITT population, FF/100 mcg resulted in a numerically lower rate of exacerbations versus FF 200 mcg containing therapies (Figure 2A). The effect of FF/200 mcg on trough FEV1 was superior to FF 100/25 mcg containing therapies.

Post hoc analyses

When all 180 mg-containing treatment groups were pooled and compared with the pooled FF 200 mcg-containing treatment groups, pooling FF data appeared to have a greater effect in patients with higher baseline blood eosinophils and higher baseline FeNO levels.

In a further post-hoc analysis, addition of UMEC 62.5 mcg was associated with further greater improvements in trough FEV1 compared with the original study treatment (Figure 2B), with a suggestion of a numerically greater reduction in the combined rate of exacerbation events at the lower range of baseline FeNO levels.

Table 1. Baseline demographic and clinical characteristics of subjects included according to baseline blood eosinophil and FeNO measurement.

Results

Conclusion

The CAPTAIN study was designed to explore the potential to reduce exacerbation rates in patients with type 2 inflammatory biomarkers.

The low number of severe exacerbation events in the low and high combined biomarker groups may have limited the statistical power to detect a difference in exacerbation rates.

Inconsistencies in the effect of adding UMEC in the unpooled analysis of moderate/severe exacerbations was noted between treatment groups.

Conclusions

The addition of UMEC improved trough FEV1, independently of baseline blood eosinophil and FeNO levels.

The effect of increasing the dose of FF on trough FEV1 and exacerbation rates was associated with higher blood eosinophil counts and FeNO levels.

This conclusion was partially confirmed, for the combined measure of blood eosinophils and FeNO, for the FF/200 mcg-containing therapies, suggesting that blood eosinophils at a cut-off of 1.2 x 10⁶ cells/L on a number of occasions and/or of FeNO measurements at a level of ≥25 parts per billion are diagnostic of type 2 inflammation.

Data on file, and unpublished.

Prepared for the American Thoracic Society Annual Meeting (2020)