EE253

Comparative Efficacy of Beclomethasone/Formoterol/Glycopyrronium (BDP/FOR/GLY) Vs Budesonide/Glycopyrrolate/Formoterol (BUD/GLY/FOR): Indirect Comparison in Chinese Patients with Chronic Obstructive Pulmonary Disease

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Introduction

- Although the comparative efficacy of single-inhaler triple therapies (SITT) in patients with moderate to severe chronic obstructive pulmonary disease (COPD) has been demonstrated[1], the comparative efficacy between SITTs in the Chinese COPD patient population remains unclear.
- This study performed an indirect treatment comparison (ITC) of the efficacy of the extra fine SITT with beclomethasone / formoterol / glycopyrronium bromide (BDP/FOR/GLY) versus budesonide / glycopyrrolate / formoterol (BUD/GLY/FOR) in Chinese COPD patients.

Methods

Systematic literature review

- A systematic literature review (SLR) was performed to identify clinical evidence for interventions of moderate-to-severe COPD published between 2016 and January 2021.
- The SLR identified 18 randomized clinical trials, six of which were relevant for the comparison between BDP/FOR/GLY (TRINITY[2], TRIBUTE[3], TRILOGY[4], TRIVERSYTI[5]) and BUD/GLY/FOR (KRONOS[6], ETHOS[7]).
- Study design, baseline characteristics, and outcome measures of these studies were compared in a heterogeneity assessment.
- The heterogeneity assessment identified TRIVERSYTI and KRONOS as best candidates for an ITC in Chinese patients with moderate-to-severe COPD.

Indirect treatment comparison

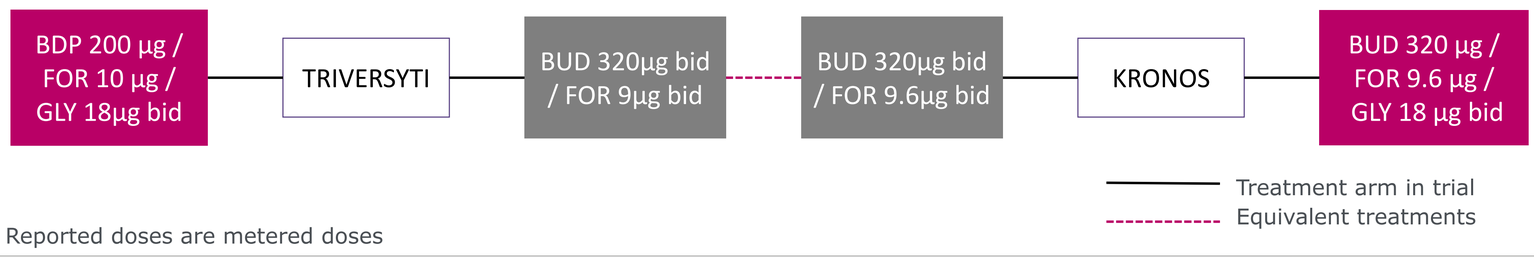
- A Bucher ITC was performed on the TRIVERSYTI and KRONOS studies[8], in line with the guidance published by the National Institute for Health and Care Excellence[9].
- The Bucher ITC methodology can be used for a simple indirect comparison where interventions are compared to a common comparator[10]. The network of the ITC is presented in Figure 1.
- Rate ratios (RR) and mean differences (MD) along with 95% confidence intervals (CI) were calculated for binary and continuous outcomes, respectively.

Results

- The outcomes for which comparisons were feasible in the Chinese population were the rate of moderate or severe exacerbations, rate of pneumonia, number of patients with pneumonia, mortality rate, and FEV1 change from baseline (CFB) at week 24.
- Due to low number of deaths observed in the intervention arms of KRONOS and TRIVERYTI (0 and 1, respectively), limiting the interpretation of the results, mortality was not presented.
- Definition for pneumonia was not available for TRIVERSYTI. FEV1 outcomes were reported based on a linear mixed model for repeated measures for TRIVERSYTI, and based on least squares mean difference for KRONOS.

Methods (continued)

Figure 1. Network used for the Bucher indirect treatment comparison.



Results (continued)

- In absence of follow-up years reported in KRONOS the follow-up per patient was assumed to be half of the KRONOS study duration. This assumption was tested in a sensitivity analysis where the mean follow-up per patient was assumed to be equal to TRIVERSYTI.
- Age, proportion of males, and smoking status were comparable between the two studies (Table 1).
- Differences were observed in the pack-years smoked, exacerbations in previous year, proportion receiving ICS/LABA, and FEV1 predicted (Table1).

Table 1. Baseline characteristics

Variables	TRIVERSYTI		KRONOS	
	BDP 200µg / FOR 10µg / GLY 18µg bid	BUD 320µg / FOR 9µg bid	BUD 320µg / FOR 9.6µg / GLY 18µg bid	BUD 320µg / FOR 9.6µg bid
Mean age, years	65.3	65.3	63.8	63.7
Years since diagnosis	6.3	5.8	4.7	5.1
Exacerbations in the last year	1: 76.2% 2+: 23.7%	1: 77.9% 2+: 22.0%	1: 27.1% 2+: 9.7%	1: 22.2% 2+: 12.5%
% male	94.8	94.1	95.8	84.7
Current smoker	24.8%	25.9%	27.8%	27.8%
Smoking history (pack-years)	39.0	40.8	35.0	30.0
FEV1 (%predicted)	34.1%	33.5%	47.9%	48.5%
ICS/LABA at baseline	73.8%	76.2%	56.3%	56.9%

Base case

- BDP/FOR/GLY demonstrated numerical improvements versus BUD/GLY/FOR in moderate or severe exacerbations (RR: 0.575, CrI [0.247, 1.336]), and pneumonia (pneumonia cases RR: 0.753, CrI [0.086, 6.599]; pneumonia events RR: 0.942, CrI [0.112, 7.88]) (Figure 2).
- BDP/FOR/GLY was associated with a lower FEV_1 CFB versus BUD/GLY/FOR (MD: -5ml, CI: [-55.351, 45.351]), but the CI did not cross the clinically important difference of 100ml, suggesting non-inferiority of BDP/FOR/GLY.

Sensitivity analysis

- Results of the sensitivity analysis were congruent with the base case, suggesting that BDP/FOR/GLY is numerically more effective in reducing the incidence of exacerbations and pneumonia
- Similar to the base case, wide CrIs indicated high uncertainty in the results.
- FEV1 CFB was unaffected by the sensitivity analysis.

Results (continued)

Figure 2. Forest plot – base case (binary outcomes)

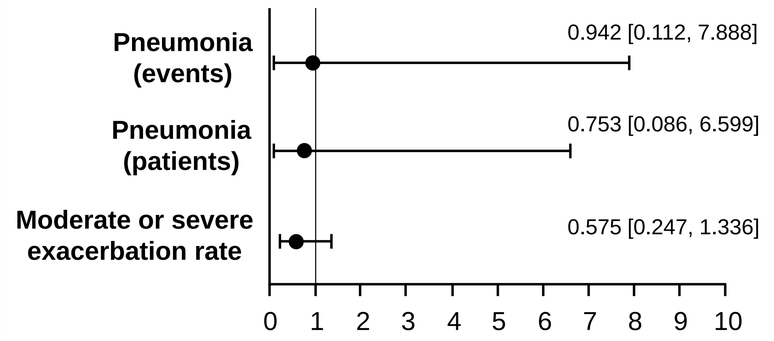
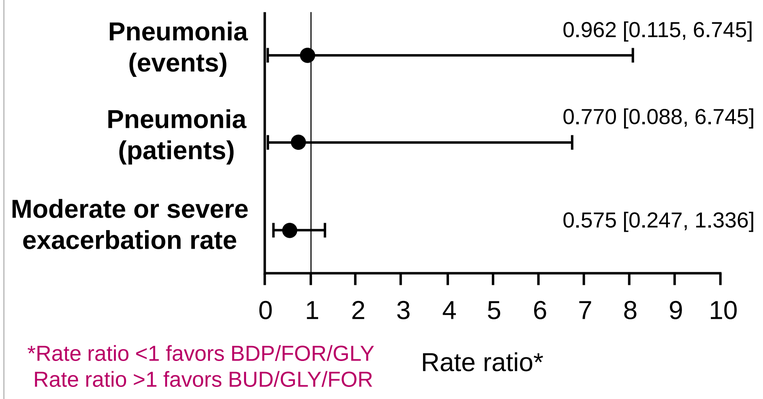


Figure 3. Forest plot – sensitivity analysis (binary outcomes)



Conclusions

Despite the inherent limitations of ITCs and uncertainties, this study demonstrated numerically greater improvement in patient-centred outcomes for BDP / FOR / GLY versus BUD/GLY/FOR in the Chinese population.

References

1. Ismaila AS, et al. *Adv Ther.* 2022;39(9):3957-3978
2. Vestbo J, et al. *Lancet.* 2017;389(10082):1919-1929.
3. Papi A, et al. *Lancet*. 2018;391(10125):1076-1084.
4. Singh D, et al. *Lancet*. 2016;388(10048):963-973.
5. Zheng J, et al. *Respir Res*. 2021;22(1):90.
6. Ferguson GT, et al. *Lancet Respir Med*. 2018;6(10):747-758.
7. Rabe KF, et al. *N Engl J Med*. 2020;383(1)35-48.
8. Bucher HC, et al. *J Clin Epidemiol*. 1997;50(6):683-691.
9. NICE Decision Support Unit. TSD 2. 2016.
10. Bucher HC, et al. Clin Epidemiol. 1997; 50(6):683-91.

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