Belcomethasone/Formoterol/Glycopyrronium vs. Fixed and Open Combinations of Inhaled Corticosteroids, Long-Acting B2-Agonist and Long-Acting Muscarinic Antagonist in Adults with Uncontrolled Asthma: a Network Meta-Analysis

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Introduction

- Asthma is a chronic, highly prevalent respiratory disease affecting 357 million people worldwide.[1]
- Patients with moderate or severe asthma who are adherent to treatment with inhaled corticosteroid (ICS) plus long-acting β2-agonist (LABA) often still have uncontrolled disease.[2]
- Single inhaler triple therapy (SITT), such as beclomethasone / formoterol / glycopyrronium bromide (BDP/FOR/GLY) is recommended as an option for patients who remain uncontrolled on inhaled corticosteroids plus long-acting β2-agonists (ICS/LABA).[3]
- The superiority of SITT over dual inhaler therapies in reducing the rate of exacerbations for patients with uncontrolled asthma has previously been demonstrated.[5,6] However, limited evidence exists on the comparative efficacy between triple therapy combinations.

Study objective: **To estimate the comparative efficacy of SITT and open triple therapies for patients with uncontrolled asthma despite treatment with medium-strength (MS) or high-strength (HS) ICS/LABA.**

Methods

Systematic literature review: A systematic literature review (SLR) was conducted to identify randomized control trials in adult patients with uncontrolled asthma. The SLR identified 5,110 records out of which 33 were considered for the NMA. Following heterogeneity assessment and exclusion of studies with patients receiving single ICS at baseline, as a predictor of less severe asthma, six studies informed the NMA networks.

Outcomes and interventions: Outcomes of interest included annualized rates of severe and moderate-to-severe exacerbations due to their clinical and economic importance. Interventions of interest included ICS/LABA and single inhaler or open triple therapies for patients with uncontrolled asthma.

Networks: Separate networks were constructed for patients previously treated with MS and HS ICS after the feasibility assessment established the plausibility of the transitivity assumption and connected networks (Figure 1, Figure 2). MD and HD ICS classification was based on GINA guidelines.[2]

Statistical methods: A Bayesian NMA was performed using Hamiltonian Monte Carlo. A Poisson likelihood with log link was considered for reported outcomes (i.e., exacerbation rates), while both fixed-effects (FE) and random effects (RE) models were fit to the data. Model selection was performed based on the posterior mean residual deviance and the deviance information criterion (DIC). An inconsistency assessment was implemented to networks with closed loops.

Outcomes were presented as rate ratios (RR) and 95% Credible Intervals (CrI) were calculated.

Results

MS network: MS BDP/FOR/GLY reduced *severe exacerbations* compared to MS ICS/LABA and MS fluticasone/umeclinidium/vilanterol (FF/UMEC/VI). MS BDP/FOR/GLY was also numerically favourable compared with MS indacaterol/ glycopyrronium/ mometasone (IND/GLY/MF), whereas it showed a similar effect to HS ICS/LABA.

In *moderate-to-severe exacerbations*, MS BDP/FOR/GLY was superior to MS ICS/LABA and similar to HS ICS/LABA, MS FF/UMEC/VI, and MS IND/GLY/MF with no statistically significant differences.

HS network: HS BDP/FOR/GLY significantly reduced *severe exacerbations* compared to MS ICS/LABA, HS ICS/LABA, MS IND/GLY/MF, and MS FF/UMEC/VI, while resulted in numerical improvements compared with HS IND/GLY/MF, salmeterol/ fluticasone + tiotropium (SALM/FF+TIO), and HS FF/UMEC/V. BDP/FOR+TIO was numerically superior to HS BDP/FOR/GLY, not reaching statistical significance.

In *moderate-to-severe exacerbations*, HS BDP/FOR/GLY established superiority over MS ICS/LABA, HS ICS/LABA, MS IND/GLY/MF, and MS FF/UMEC/VI and was found numerically favorable to SALM/FF+TIO. Compared to BDP/FOR +TIO, HS BDP/FOR/GLY was numerically unfavorable and showed similar effect with HS IND/GLY/MF.

Conclusions

Compared to relevant SITTs and open triple therapies, MS and HS BDP/FOR/GLY are associated with a statistically significant clinical benefit or numerical differences in the rate of severe and moderate-to-severe asthma exacerbations.

Figure 1. Network of evidence of MS for severe and moderate-to-severe asthma exacerbations.

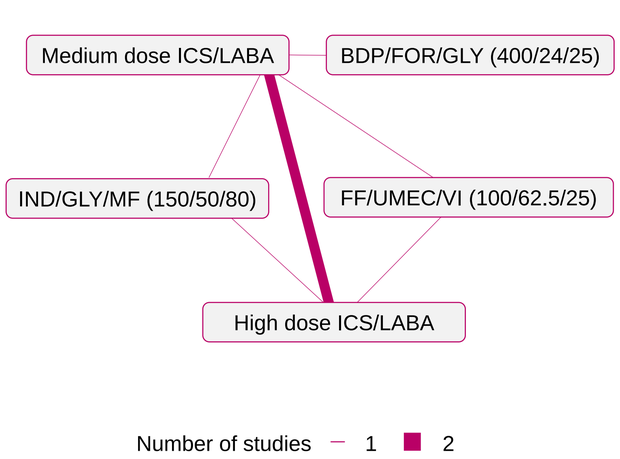
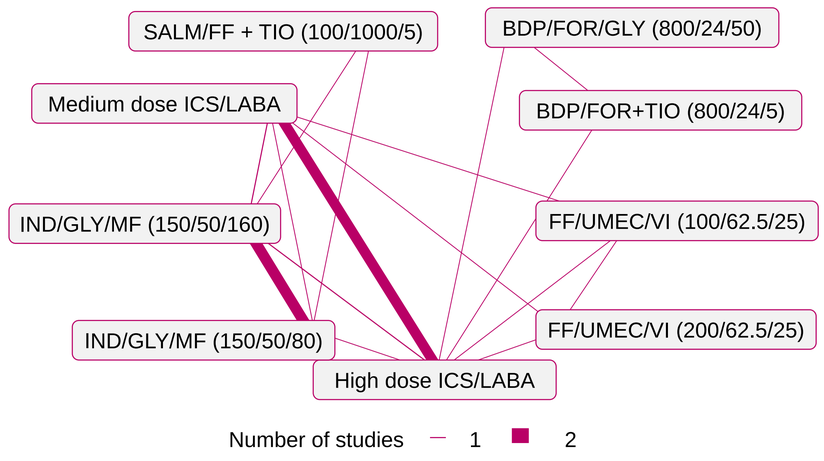
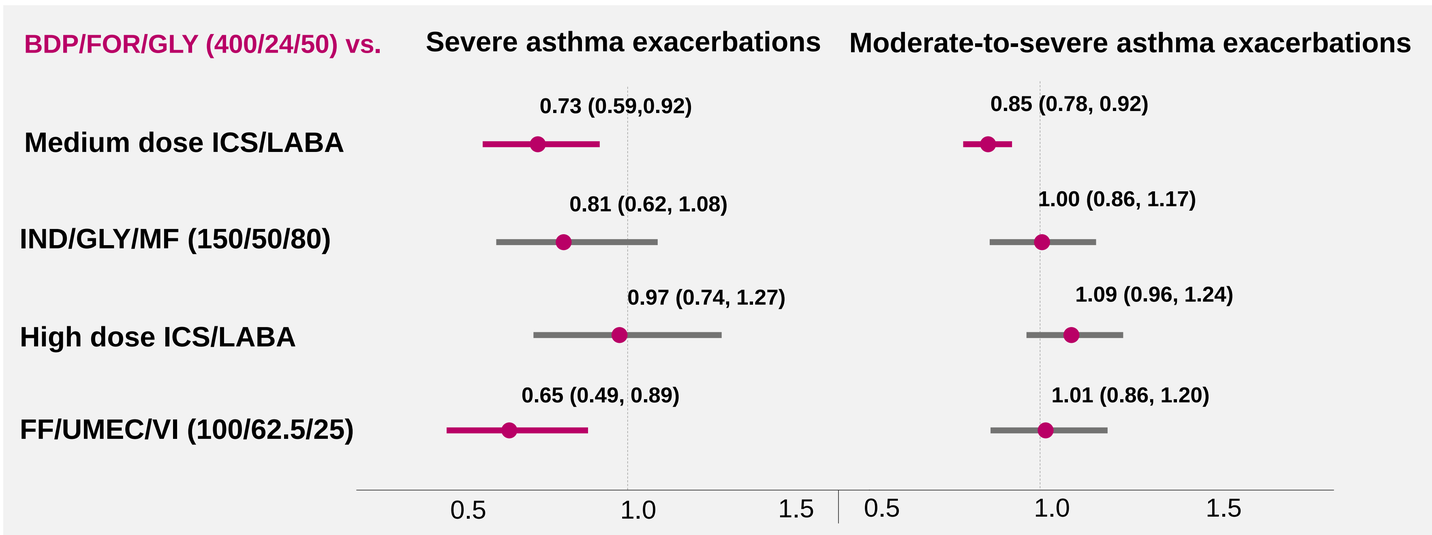


Figure 2. Network of evidence of HS for severe and moderate-to-severe asthma exacerbations.



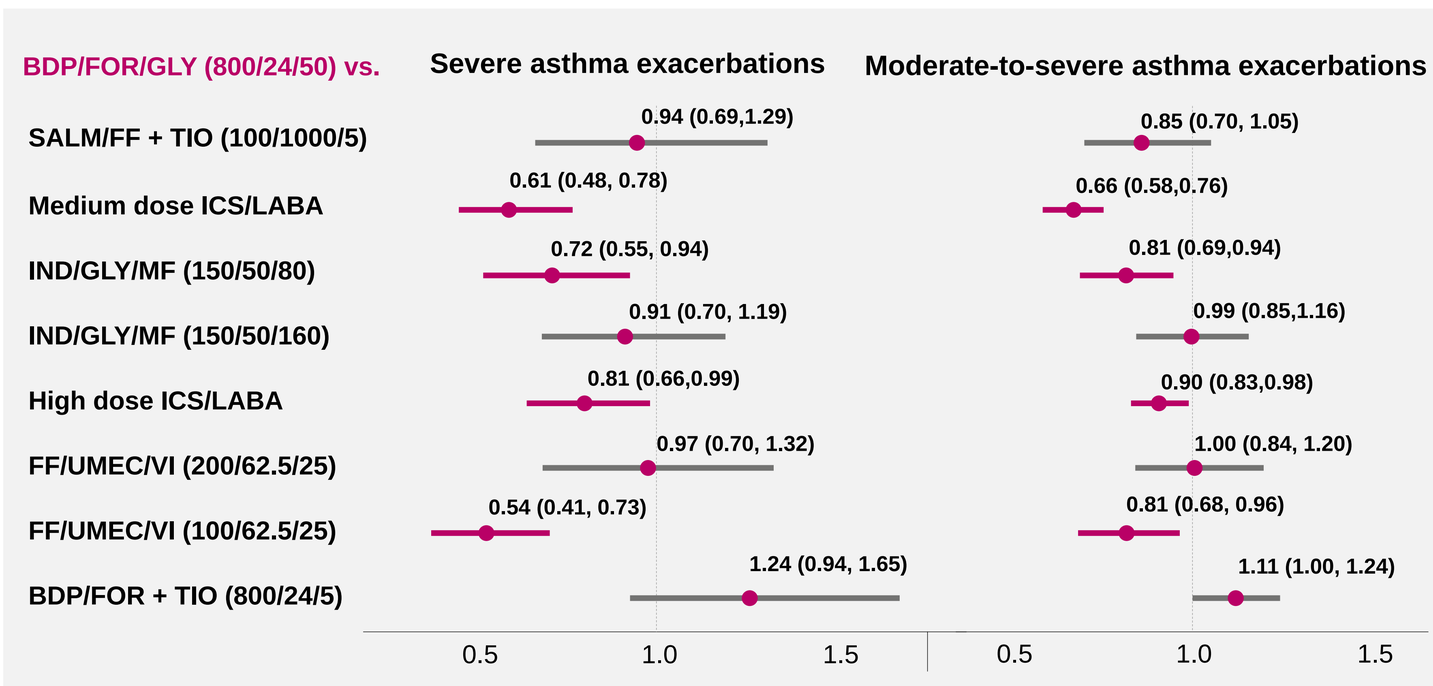
Abbreviations: BDP: beclomethasone ; FOR: formoterol ; FF: fluticasone; GLY: glycopyrronium; ICS: inhaled corticosteroids; LABA: long-acting β2-agonists; MF: mometasone; SALM: salmeterol; TIO: tiotropium ; UMEC: umeclinidium; VI: vilanterol;

Figure 3. Forest plot of relative efficacy of BDP/FOR/GLY (400/24/25) in the analysis severe and moderate-to-severe asthma exacerbation rate



Abbreviations: BDP: beclomethasone ; FOR: formoterol ; FF: fluticasone; GLY: glycopyrronium; ICS: inhaled corticosteroids; LABA: long-acting β2-agonists; MF: mometasone; UMEC: umeclinidium; VI: vilanterol.

Figure 4. Forest plot of relative efficacy of BDP/FOR/GLY (800/24/25) in the analysis severe and moderate-to-severe asthma exacerbation rate



Abbreviations: BDP: beclomethasone ; FOR: formoterol ; FF: fluticasone; GLY: glycopyrronium; ICS: inhaled corticosteroids; LABA: long-acting β2-agonists; MF: mometasone; UMEC: umeclinidium; VI: vilanterol.

References

1. Song P, et al. J Glob Health. 2022 Jun 29:12:04052
2. Sulaiman I., et al Eur Respir J. 2018 Jan 4;51(1):1701126.
3. Global Initiative for Asthma (GINA) (2023). Global strategy for asthma management and prevention.(accessed 3 May 2023).
4. Higgins et al. BMJ. 2011 Oct 18:343:d5928
5. Kim L., et al. JAMA. 2021 Jun 22;325(24):2466-2479
6. Rogliani P., et al. Eur Respir J. 2021 Sep 2;58(3):2004233