

# Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial

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## SUMMARY

**Background** Exacerbations of asthma cause a substantial global illness burden. Adults with uncontrolled persistent asthma despite maintenance treatment require additional therapy. Since macrolide antibiotics can be used to treat persistent asthma, we aimed to assess the efficacy and safety of oral azithromycin as add-on therapy in patients with uncontrolled persistent asthma on medium-to-high dose inhaled corticosteroids plus a long-acting bronchodilator.

**Methods** We did a randomised, double-blind, placebo controlled parallel group trial to determine whether oral azithromycin decreases the frequency of asthma exacerbations in adults ( $\geq 18$  years) with symptomatic asthma despite current use of inhaled corticosteroid and long-acting bronchodilator, and who had no hearing impairment or abnormal prolongation of the corrected QT interval. Patients were randomly assigned (1:1) to receive azithromycin 500 mg or placebo three times per week for 48 weeks. Patients were centrally allocated using concealed random allocation from a computer-generated random numbers table with permuted blocks of 4 or 6 and stratification for centre and past smoking. Primary efficacy endpoints were the rate of total (severe and moderate) asthma exacerbations over 48 weeks and asthma quality of life. Data were analysed on an intention-to-treat basis. The trial is registered at the Australian and New Zealand Clinical Trials Registry (ANZCTR), number 12609000197235.

**Findings** Between June 12, 2009, and Jan 31, 2015, 420 patients were randomly assigned (213 in the azithromycin group and 207 in the placebo group). Azithromycin reduced asthma exacerbations (1.07 per patient-year [95% CI 0.85–1.29]) compared with placebo (1.86 per patient-year [1.54–2.18]; incidence rate ratio [IRR] 0.59 [95% CI 0.47–0.74];  $p < 0.0001$ ). The proportion of patients experiencing at least one asthma exacerbation was reduced by azithromycin treatment (127 [61%] patients in the placebo group vs 94 [44%] patients in the azithromycin group,  $p < 0.0001$ ). Azithromycin significantly improved asthma-related quality of life (adjusted mean difference, 0.36 [95% CI 0.21–0.52];  $p = 0.001$ ). Diarrhoea was more common in azithromycin-treated patients (72 [34%] vs 39 [19%];  $p = 0.001$ ).

**Interpretation** Adults with persistent symptomatic asthma experience fewer asthma exacerbations and improved quality of life when treated with oral azithromycin for 48 weeks. Azithromycin might be a useful add-on therapy in persistent asthma.

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