Azithromycin Fizzled in CF Without *P. aeruginosa*

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FROM JAMA

A 6-month course of azithromycin did not improve lung function in children and adolescents who had mild cystic fibrosis without *Pseudomonas aeruginosa* infection, according to a report.

The antibiotic failed to achieve the primary end point of improvement in forced expiratory volume in 1 second (FEV_1) in a randomized controlled trial of 263 CF patients with mild disease, and it also did not decrease the need for intravenous or inhaled antibiotics or for hospitalization.

However, azithromycin achieved the exploratory end points of reducing pulmonary exacerbations, preventing initiation of other oral antibiotics, and increasing thin patients' weight and body mass index.

"Further studies of azithromycin are warranted to further investigate its potential use in this population," said Dr. Lisa Saiman of the pediatrics department at Columbia University, New York, and her associates (JAMA 2010;303:1707-15).

Azithromycin has both antimicrobial and anti-inflammatory activity, although its exact mechanism of action in CF is not yet known. It is recommended as chronic therapy for CF patients infected with *P. aeruginosa*, but its use in children who do not have *P. aeruginosa* has not been well studied.

Dr. Saiman and her colleagues assessed the drug in relatively healthy CF patients aged 6-18 years who had an FEV_1 of at least 50% predicted and had negative cultures for *P. aeruginosa*. The study subjects were treated between 2007 and 2009 at 40 centers accredited for CF care throughout the United States and Canada.

The patients were randomly assigned to receive 2-3 daily azithromycin tablets (131 patients) or a matching placebo (132 patients) for 168 days, and were closely followed for 196 days. Adherence in the treatment and placebo groups was 90% and 91%, respectively, and only eight participants (five on active treatment and three on placebo) withdrew from the study.

VITALS

Major Finding: Mean FEV_1 was 2.13 at baseline and 2.22 at 6 months with the active drug, compared with 2.12 at baseline and 2.20 at 6 months with placebo.

Data Source: A 6-month placebo-controlled study of azithromycin in 263 relatively healthy children and adolescents with CF who had negative cultures for *P. aeruginosa*.

Disclosures: CF Foundation Therapeutics Inc. funded the study, and Pfizer Inc. supplied the azithromycin and the placebo. Dr. Saiman reported ties to Pfizer Inc., maker of azithromycin, and Aridis Pharmaceuticals LLC, Bayer, CF Foundation Therapeutics Inc., Chiesi Pharmaceuticals Inc., Gilead Sciences Inc., Johnson & Johnson, Mpex Pharmaceuticals Inc., Novartis, SmithKline Beecham Inc., and Transave Inc.

Azithromycin did not improve FEV_1, compared with placebo. Mean FEV_1 was 2.13 at baseline and 2.22 at 6 months with the active drug, compared with 2.12 at baseline and 2.20 at 6 months with placebo. Similarly, azithromycin failed to improve other indicators of pulmonary function, such as forced vital capacity and forced midexpiratory flow rate. There were no differences between the treatment and placebo groups in the number of hospitalizations or the need for IV or inhaled antibiotics.

However, azithromycin decreased the number of pulmonary exacerbations by nearly half and the need for new oral antibiotics by 27%, compared with placebo. It was also associated with a significant weight gain (0.58 kg) and a significant increase in body mass index (0.34 units).

The drug was well tolerated, producing no increase in the rates of nausea, diarrhea, wheezing, and serious or nonserious adverse events, compared with placebo.

The only significant differences between the two groups in treatment-emergent pathogens were found with macrolide-resistant *Staphylococcus aureus* and *Haemophilus influenzae*. Azithromycin users had 27% and 7% more emergence of those organisms, respectively, than did placebo participants. ■