

## COPD Exacerbations and Hospitalizations

Patients do not recover fully from COPD exacerbations. Patients with more frequent or severe COPD exacerbations have rapid declines in lung function and overall health, often leaving patients unable to leave their homes.

COPD is the **3rd leading cause** = **150,000** deaths per year of death per year in the U.S.

COPD causes **700,000** hospitalizations each year  
 Rehospitalization rate of patients  
**20%** at 1 mo. **30%** at 3 mos. **40%** at 12 mos.

### Proven to prevent COPD exacerbations in patients with chronic bronchitis

## Azithromycin

An antibiotic with anti-inflammatory properties; a macrolide antibiotic

Recommended by 2015 ACCP/CTS guidelines<sup>1</sup>  
 Recommended by 2017 GOLD guidelines<sup>2</sup>  
 Recommended by 2017 ERS/ATS guidelines<sup>3</sup>

## Roflumilast Daliresp®

Non-corticosteroid oral anti-inflammatory medication; phosphodiesterase type 4 (PDE4) inhibitor

Recommended by 2015 ACCP/CTS guidelines<sup>1</sup>  
 Recommended by 2017 GOLD guidelines<sup>2</sup>  
 Recommended by 2017 ERS/ATS guidelines<sup>3</sup>  
 FDA-approved for prevention of COPD exacerbations<sup>4</sup>

### Average reduction in yearly exacerbation rates, as compared to placebo








**5–28%**

95% confidence interval<sup>5</sup>

**7–19%**

Pooled 95% confidence interval<sup>6,7,8</sup>

### Side effects in comparative trials of up to 12 months

Azithromycin 250 mg per day <sup>5</sup> n = 558 placebo = 559	Roflumilast 500 mcg per day <sup>6,7,8</sup> n = 3,693 placebo = 3,686
 <b>Hearing reduction</b> 25% v 20% placebo	 <b>GI effects (diarrhea)</b> 17% v 6% placebo
 <b>QTc prolongation</b> 1% v 0.7% placebo	 <b>Weight loss</b> 9% v 3% placebo
 <b>Stopped treatment for side effects</b> 33% v 28% placebo	 <b>Stopped treatment for side effects</b> 12% v 8% placebo
 <b>Macrolide resistance</b> 81% v 41% placebo (38/47) v (44/108)	FDA prescribing information suggests starting at 250 mcg / day X 4 weeks to reduce rate of treatment discontinuation; <sup>4,9</sup>

### Some other side effects reported in FDA prescribing information<sup>4,10</sup>

Cardiac dysrhythmias, diarrhea, nausea, hepatotoxicity, vomiting, dizziness, vaginitis, dyspepsia

Headaches, insomnia, anxiety, depression, suicidal thoughts or other mood changes

### Contraindications<sup>4,10</sup>

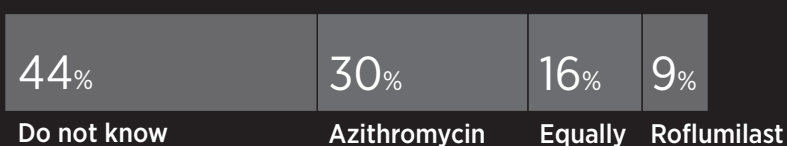
History of cholestatic jaundice/hepatic dysfunction associated with prior use of azithromycin  
 Hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide drug

Moderate to severe liver impairment (Child-Pugh B or C)

## Which drug is best for whom?

Results of clinical trials indicate that either azithromycin or roflumilast are effective at reducing COPD exacerbations. What we don't know is which drug is better for which type of patient. Pulmonologists with expertise in treating COPD have different opinions about which treatment is best, and many reported they don't know.<sup>11</sup>

n=43 pulmonologists



The RELIANCE study is designed to evaluate the relative benefits and harms of azithromycin and roflumilast. RELIANCE seeks to understand which treatment is most likely to:

- Improve hospital-free survival (primary outcome)
- Improve social, physical, and mental health
- Reduce the risk of future COPD exacerbations
- Support Hospital Readmissions Reduction Programs
- Better for current and past smokers with COPD and chronic bronchitis hospitalized in the past 12 months



Funded by Patient-Centered Outcomes Research Institute (PCORI)

(Roflumilast or Azithromycin to prevent COPD Exacerbations)

<sup>1</sup><http://journal.publications.chestnet.org/article.aspx?articleID=1918413>

<sup>2</sup>Global Initiative for Chronic Obstructive Lung Disease. <http://www.goldcopd.org>. Accessed 3/5/2017

<sup>3</sup>Wedzicha JA, Calverley PMA, Albert RK, et al. Prevention of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J 2017; 50: 1602265

<sup>4</sup>[https://www.azpicentral.com/daliresp/daliresp\\_med.pdf#page=1](https://www.azpicentral.com/daliresp/daliresp_med.pdf#page=1) (accessed Feb 2, 2018)

<sup>5</sup>MACRO, 2011. Albert RK, NEJM 2011; 365: 689-698

<sup>6</sup>RE2SPOND, 2016. Martinez FJ, Am J Respir Crit Care Med; 194: 559-567

<sup>7</sup>REACT, 2015. Martinez FJ, Lancet; 385: 857-866

<sup>8</sup>M2-124 and M2-125 Study Groups, 2009. Calverley PMA, Lancet; 374: 685-94

<sup>9</sup>OPTIMIZE, 2016. Watz H, ERS International Congress abstract

<sup>10</sup>[http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2017/050710s44-050711s41-050784s28tbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2017/050710s44-050711s41-050784s28tbl.pdf)

<sup>11</sup>RELIANCE Trial, 2016. Krishnan, JA, ATS International Conference abstract