COPD Exacerbations and Hospitalizations

Patients do not fully recover 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
of death per year in the U.S.

= 150,000
deaths per year

COPD causes
700,000
hospitalizations each year

Rehospitalization rate of patients
20% at 1 mo.
30% at 3 mos.
40% at 12 mos.

Oral therapies 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[1]
Recommended by 2017 GOLD guidelines[2]

Roflumilast Daliresp®

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

Recommended by 2015 ACCP/CTS guidelines[1]
Recommended by 2017 GOLD guidelines[2]
FDA approved for prevention of COPD exacerbations

Average reduction in yearly exacerbation rates, as compared to placebo

5-46%
Pooled 95% confidence interval[3,4]

5-19%
Pooled 95% confidence interval[6,7,8]

Side effects in comparative trials of up to 12 months

	Azithromycin	Roflumilast
	[3,4,5]250-500mg every 1-2 days n = 752 placebo = 758	500 mcg per day[6,7,8] n = 3,711 placebo = 3,686
	[3,5]**Hearing reduction** 20% v 16% placebo	**GI effects (diarrhea)**[6,7,8] 9% v 3% placebo
	[3,5]**QTc prolongation** 1% v 0.7% placebo	**Weight loss**[6,7,8] 9% v 3% placebo
	[3,4,5]**Stopped treatment for side effects** 26% v 22% placebo	**Stopped treatment for side effects**[6,7,8] 12% v 8% placebo
	[3,4,5]**Macrolide resistance** 43% v 36% placebo	*Treatment discontinuation from Adverse Effects may be lower by starting with Roflumilast 250 mcg once a day or 500 mcg every other day for 4 weeks*[9]

Some other side effects reported in FDA prescribing information[10,11]

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

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

Contraindications[10,11]

History of cholestatic jaundice/hepatic dysfunction associated with prior use of azithromycin

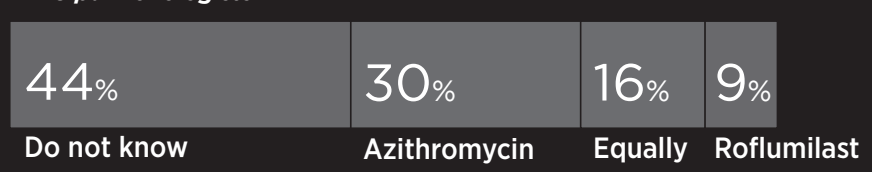
Hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide drug

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.[12]

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

RELIANCE
(RofLumilast or Azithromycin to preveNt COPD Exacerbations)

Funded by Patient-Centered Outcomes Research Institute (PCORI)

[1] http://journal.publications.chestnet.org/article.aspx?articleID=1918413
[2] Global Initiative for Chronic Obstructive Lung Disease. http://www.goldcopd.org. Accessed 3/5/2017
[3] MACRO, 2011. Albert RK, NEJM 2011; 365: 689-698
[4] COLUMBUS, 2014. Uzun S, Lancet Respir Med; 2: 361-368.
[5] BACE, 2019. Vermeersch, K, AJRCCM; 10.1164/rccm.201901-0094OC
[6] RE2SPOND, 2016. Martinez FJ, Am J Respir Crit Care Med; 194: 559–567
[7] REACT, 2015. Martinez FJ, Lancet; 385: 857-866
[8] M2-124 and M2-125 Study Groups, 2009. Calverley PMA, Lancet; 374: 685–94
[9] OPTIMIZE, 2016. Watz H, ERS International Congress abstract
[10] http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022522s006lbl.pdf
[11] http://www.accessdata.fda.gov/drugsatfda_docs/label/2017/050710s44-050711s41-050784s28lbl.pdf
[12] RELIANCE Trial, 2016. Krishnan, JA, ATS International Conference abstract