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.

Rehospitalization rate of patients

<table>
<thead>
<tr>
<th>COPD causes</th>
<th>Rehospitalization rate of patients</th>
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</thead>
<tbody>
<tr>
<td>700,000</td>
<td>20% at 1 mos.</td>
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<tr>
<td></td>
<td>30% at 3 mos.</td>
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<tr>
<td></td>
<td>40% at 12 mos.</td>
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20% at 1 mo. 30% at 3 mos. 40% at 12 mos.

700,000 hospitalizations each year

150,000 deaths per year

COPD is the 3rd leading cause of death per year in the U.S.

COPD Exacerbations and Hospitalizations

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

Recommended by 2017 GOLD guidelines

Average reduction in yearly exacerbation rates, as compared to placebo

Azithromycin: 5.46% (Pooled 95% confidence interval)

Roflumilast: 5.19% (Pooled 95% confidence interval)

Side effects in comparative trials of up to 12 months

- **Azithromycin**:
  - GI effects (diarrhea): 9% v 3% placebo
  - QTc prolongation: 1% v 0.7% placebo
  - Stopped treatment for side effects: 26% v 22% placebo

- **Roflumilast**:
  - Weight loss: 9% v 3% placebo
  - Stopped treatment for side effects: 12% v 8% placebo

Some other side effects reported in FDA prescribing information

- Hearing reduction: 20% v 16% placebo
- GI effects (diarrhea): 9% v 3% placebo
- QTc prolongation: 1% v 0.7% placebo
- Stopped treatment for side effects: 26% v 22% placebo
- Macrolide resistance: 43% v 36% placebo

Contraindications

- 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)

Clinical equipoise: 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.

Roflumilast Daliresp®

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

Recommended by 2015 ACCP/CTS guidelines

Recommended by 2017 GOLD guidelines

FDA approved for prevention of COPD exacerbations

**Clinical equipoise:** 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.

44%

30%

16%

9%

Do not know

Azithromycin

Equally

Roflumilast

n=43 pulmonologists

1http://journal.publications.chestnet.org/article.aspx?articleID=1918413
9OPTIMIZE, 2016. Watz H, ERS International Congress abstract
10http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/022522s006lbl.pdf
11http://www.accessdata.fda.gov/drugsatfda_docs/label/2017/050710s44-050711s41-050784s28lbl.pdf
12RELIANCE Trial, 2016. Krishnan, JA, ATS International Conference abstract

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