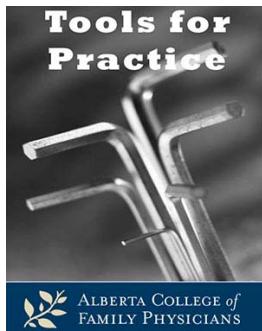


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Roflumilast – COPD relief at last?

Clinical Question: Is roflumilast (Daxas®) beneficial as an add-on therapy in the management of COPD?

Evidence:

2011 Cochrane systematic review¹ of 9 trials (9211 patients) of roflumilast, which includes the two most significant publications (with two trials each).^{2,3} Findings:

- Statistically significant benefit:
 - Reduced likelihood of 1 or more COPD exacerbations (requiring corticosteroid or admission)¹: 24.1% in placebo versus 20.8% in roflumilast, Number Needed to Treat (NNT) 31
- Not statistically and/or clinically significant:
 - Statistically but not clinically significant improvement in FEV(1) with roflumilast (54 mL)¹
 - Multiple quality of life and symptoms scores with few reaching statistical significance and none reaching clinical significance¹⁻³
 - No difference in overall mortality¹
- Harms:
 - More participants in the roflumilast groups experienced weight loss (NNH 15), diarrhea (NNH 17), nausea (NNH 34), and headache (NNH 50).¹
 - Weight loss appears to be approximately 2kg over 24²-52³ weeks.

Context:

- Roflumilast is the first oral phosphodiesterase 4 (PDE(4)) inhibitor to be approved in Canada for COPD management.⁴ Its proposed mechanism of action is a reduction in the airway inflammation and bronchoconstriction seen in COPD.
- Change in FEV1 of 100 mL is considered the minimum clinically important difference.⁵
 - However, the observed FEV1 improvement with roflumilast is similar to that for salmeterol or fluticasone in the TORCH trial.⁶
- In patients who have previously been hospitalized because of COPD, being underweight or experiencing weight loss is related to a higher risk of exacerbations.⁷

Bottom-line: The present evidence suggests that roflumilast is beneficial for improvement of exacerbations. However, benefits in other clinical outcomes including quality of life and mortality are not demonstrated and harms such as weight loss, headache and gastrointestinal irritation are common. The net benefit of roflumilast is questionable and long-term effectiveness is unclear.

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