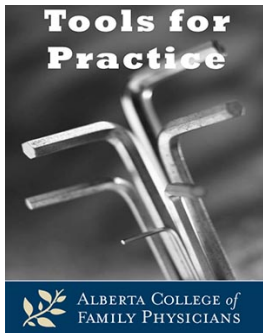


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Evidence Updated: New evidence, context updated
Bottom Line: Slight change
First Published: April 30, 2012



Which is the best puffer for initial therapy in COPD?

Clinical Question: Which puffer has the greatest impact on clinical outcomes as the first-line long-acting inhaled treatment for COPD?

Bottom Line: Tiotropium (or other LAMA) +/- LABA is the best initial long-acting therapy for COPD, followed by a LABA (like salmeterol). Despite widespread use, inhaled steroids increase pneumonia risk and provide little if any benefit in COPD.

Evidence:

- Long-acting antimuscarinic agents (LAMA) versus long-acting beta agonists (LABA):
 - Cochrane review¹ of seven Randomized Controlled Trials (RCTs) of 12,123 patients comparing tiotropium to LABA (formoterol, indacaterol, salmeterol) over 3-12 months.
 - More patients exacerbation-free with tiotropium: 72.7% versus 70.5% with LABA, Number Needed to Treat (NNT)=46.
 - INVIGORATE:² One year RCT (3,444 patients) randomized to tiotropium 18 mcg or indacaterol 150 mcg, each once daily.
 - More patients exacerbation-free with tiotropium: 65% versus 60% with indacaterol, NNT=20.
 - No difference in mortality or quality of life.^{1,2}
- LAMA versus LABA plus steroid:
 - INSPIRE:³ Two year trial (1,323 patients) comparing tiotropium 18 mcg daily to salmeterol/fluticasone 50/500 mcg BID.
 - No difference in exacerbations, and no clinical difference in quality of life.
 - While there were differences in some secondary outcomes, drop-out was high (39%) and no outcome data was collected on drop-outs.
 - Cochrane reviewers⁴ felt the results were unreliable.
- LAMA + LABA versus LABA plus steroid:
 - FLAME:⁵ One year RCT (3,362 patients) comparing indacaterol/glycopyrronium 110/50 mcg once daily versus salmeterol/fluticasone 50/500 mcg BID.
 - LAMA/LABA versus LABA/steroid had lower:
 - Exacerbation rate 0.88 (0.82-0.94).

- Risk of pneumonia: 3.2% versus 4.8%, NNT=63.
 - No difference in mortality and no clinical difference in quality of life.
- Meta-analysis of eight trials (4,392 patients) showed similar results.⁶
- LABA versus steroid:
 - Cochrane review⁷ (seven studies, 5,997 patients).
 - No difference in exacerbations and no clinical difference in quality of life.
 - Steroids caused more pneumonia, and possibly increased mortality (odds ratio 1.17, 95% CI 0.97-1.42).

Context:

- Most trials above were industry funded, generally favoring the sponsor's drug.
- Inhaled steroids increase the risk of pneumonia⁸ [Number Needed to Harm (NNH)=44] and fractures⁹ (NNH=83).
- Guidelines,¹⁰ written before many of these trials were published, recommend tiotropium or LABA as initial therapy.

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Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at <http://bit.ly/signupfortfp>. Archived articles are available on the ACFP website.

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