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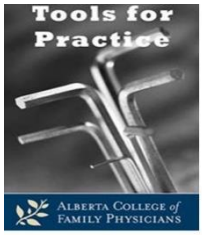
August 13, 2019



In COPD puffers, does three-of-kind beat a pair?

Clinical Question: In Chronic Obstructive Pulmonary Disease (COPD) patients on Long-Acting Muscarinic Antagonist (LAMA) and Long-Acting Beta-Agonist (LABA) dual therapy, does adding inhaled corticosteroids (ICS) improve outcomes?

Bottom Line: In COPD patients with ≥1 exacerbation per year, triple therapy reduces the risk of having ≥1 exacerbations/year compared to LAMA/LABA dual therapy (one less patient for every 36) but increases the risk of pneumonia (one more patient for every 34) and costs. It is possible that higher blood eosinophil counts (>150-300 cells/µL) may help target adding ICS.

Evidence:

- 2019 systematic review: 4 randomized, controlled trials (RCTs) comparing triple versus LAMA/LABA dual therapy in 9310 patients for 24-52 weeks, usually in patients with ≥1 exacerbation/year.[1]
    - Less exacerbations with triple therapy, Rate Ratio 0.71 (0.60-0.84).
    - Clinically important quality of life improvement (2 RCTs):
        - 50% versus 44% (dual therapy), number needed to treat (NNT)=17.
    - Serious adverse events or discontinuation due to adverse events similar.
        - Patients with ≥1 pneumonia: 6.4% versus 3.9% (dual therapy), statistically significant.
- Largest RCT of above systematic review, 6221 patients on umeclidinium/vilanterol/fluticasone (triple therapy) or umeclidinium/vilanterol (LAMA/LABA dual therapy). [Vilanterol/fluticasone arm not reported here].[2] At 1 year:
    - Exacerbation rate and quality of life similar to above systematic review.
    - Patients with ≥1 exacerbation (data from sponsor, statistics by TFP authors):
        - Triple 47% versus dual therapy 50% (statistically significant, NNT=36).
    - Patients with ≥1 pneumonia: triple 7.6% versus dual therapy 4.7% (statistically significant, number needed to harm=34).
- Other systematic reviews found similar.[3,4]

Context:

- Exacerbations in RCTs defined as moderate (needing oral steroids and/or antibiotics) or severe (leading to hospitalization or death).
- Subgroup analyses suggest individuals with higher blood eosinophil counts (>150-300 cells/μL) benefit more from triple therapy, but amount of benefit is not quantifiable.[4,5]
    - Targeting treatment by eosinophils has not specifically been tested in large RCTs.
- Newest guideline suggests adding ICS in patients who develop further exacerbations on LABA/LAMA therapy (and have blood eosinophil counts ≥100cells/μL).[6]
- When withdrawing ICS from triple, there is a small (6-8% relative), but not statistically different, increase in exacerbations.[7,8]
- Average annual cost: ~$1100 for dual versus ~$1700 for triple therapy.[9]

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Disclosures:
Authors do not have any conflicts of interest to declare.

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