In preschoolers, there was no difference in the time to first exacerbation (including exacerbations of all severities) between the PRN beclo-SABA and PRN SABA groups (p = 0.88).[53]

In children, the TREXA trial did not find a statistically significant difference in the probability of an exacerbation (including exacerbations of all severities) in the PRN beclo-SABA group versus the PRN SABA group (HR 0.62, 0.37–1.05, p = 0.073).[36]

In adults, the BEST trial found a decreased percentage of patients with at least 1 exacerbation (including exacerbations of all severities) in the PRN beclo-SABA group compared to the PRN SABA group (4.92% vs 17.8%, p = 0.002).[38] There was no significant difference in the percentage of patients with at least 1 "severe" exacerbation in the PRN beclo-SABA group compared to the PRN SABA group (0% vs 3.4%, p = 0.057), although there were only 10 "severe" exacerbations in 242 patients.

3. Asthma control

In preschoolers, there was an increase in symptom-free days only when looking at weeks 9 to12 (PRN beclo-SABA 77.4 vs PRN SABA 69.5, p = 0.033), but not when looking at weeks 1 to 12 (PRN beclo-SABA 64.9 vs PRN SABA 61, p = 0.248).[53]

In children the TREXA trial showed no significant difference in the number of days with well-controlled asthma between the PRN beclo-SABA group and the PRN SABA group, with both groups having 80-90% of days with well-controlled asthma.[36]

In adults, the BEST trial found no difference in most measures of asthma control, except for a decrease in the nocturnal awakening score with PRN beclo-SABA compared to PRN SABA (0.1 vs 0.21, difference -0.1, p = 0.03).[38] There was no difference in the daytime asthma symptom score (difference -0.28, p = 0.11), rescue medication use/day (difference -0.16, p = 0.11) or symptom free days (difference 5.69, p = 0.13).

4. FEV_1

In children in the TREXA trial, there was no difference in FEV_1 between groups, or in methacholine challenge (PC20) results at week 24.[36]

In the adult BEST trial, there was a 3.89% difference in the improvement in FEV_1% predicted in the PRN beclo-SABA group versus the PRN SABA group (p = 0.005).[38]

5. Inflammation

The pediatric trial measured FeNO at baseline and then every 8 weeks starting at week 8 and did not report a difference between the PRN beclo-SABA versus PRN SABA groups, although both groups had an elevated FeNO throughout the study compared to the groups that were on daily beclomethasone.[36]

6. Safety/mortality

There was no difference in severe adverse events in any of the trials.[36,38,53] In the preschool trial there was no difference in morning salivary cortisol between the 2 groups,[53] and in the pediatric trial no difference in growth between the PRN beclo-SABA versus SABA group.[36] There was 1 serious adverse event in the adult trial, which was hemoptysis of undetermined cause in a patient on PRN beclo-SABA,[38] and 1 severe adverse event in the preschool trial in the PRN SABA group (details of event not reported).

Expert panel discussion of additional considerations and clinical judgment of risk versus benefit

Evidence for this recommendation was extrapolated from studies that included individuals with more severe asthma. The panel felt that the use of PRN ICS-SABA compared to PRN SABA was more relevant for individuals with less severe asthma, as the current standard of care for this group would be PRN SABA.

In individuals with more frequent symptoms, there is evidence from 1 RCT in those 18 years of age and older that taking an ICS each time SABA is taken reduces "severe" asthma exacerbations, improves some aspects of asthma control and improves lung function compared to PRN SABA.[38] This adult trial included a broader definition of severe exacerbations, and therefore, there is not strong evidence for the prevention of severe exacerbations when comparing these 2 regimens. Also, this trial[38] used a single inhaler containing SABA (100 mcg salbutamol) and beclomethasone^{Eur} (250 mcg). These data cannot be generalized to our setting, as there is no single inhaler containing SABA and ICS approved for use in Canada, and none of the ICS medications are approved to be used as needed. However, given that this strategy has been shown to decrease asthma exacerbations, it could be considered as a harm reduction strategy in those 18 of years and older at higher risk for exacerbations, and who cannot take daily ICS + PRN SABA or PRN bud/form.

There is limited evidence of benefit in individuals <18 years of age. For children 6-18 years of age with more frequent symptoms or a history of severe exacerbation, there was a nonsignificant trend that an ICS taken each time a SABA was taken decreases exacerbations compared to PRN SABA, with no difference in safety outcomes (of note in that trial, daily ICS significantly decreased exacerbations compared to PRN SABA).[36] In children 1-4 years of age, there was no difference in exacerbations but an improvement in some measures of asthma control, with no difference in safety outcomes.[53] However, that trial used nebulized medication, which is not the preferred modality for delivery of asthma medication in Canada (it also used a nebule that contained ICS and SABA, which is not available in Canada). Given the possibility of overuse of ICS in this patient group, the current level of evidence, and the lack of a combined ICS-SABA inhaler on the Canadian market, the panel does not recommend this strategy for individuals under 18 years of age.