Guideline topic: Pharmacological management of asthma
Evidence table 4.25: Budesonide vs Beclomethasone
Different inhaled corticosteroids (ICS) – flixotide propionate (FP) vs budesonide (BUD) Beclomethasone dipropionate (BDP).
D = Diskhaler, MDI = metered dose inhaler, n = nebulised, RPD = reservoir powder device, T = Turbohaler, V = Volumatic

Author	Year	Study type	Quality rating	Population	Outcomes measured	Effect size	Confidence intervals / p values	Comments
Barnes[1]	1998	Meta-analysis of all papers where FP given at half (or less) the mcg dose of BUD or BDP Double blind (n=8) and open (n=6) RCTs	+	Adult and paediatric studies of asthmatics of all severity except those requiring oral steroids. 1000 treated with FP 200-800mcg/day vs 980 treated with BUD 400-1600mcg/day 780 treated with FP 200-1000 mcg/day vs 804 treated with BDP 400-2000 mcg/day	Improvement in am PEFR Ratio of mean serum cortisol levels	FP vs BUD gave +11l/min FP vs BDP gave non-significant improvement in PEFR +3l/min FP: BUD ratio 1.09 nmol/L FP : BDP = 1.03 nmol/L	+7 to +15 l/min -0.9 to +15 l/min 1.03 to 1.15 0.99 to 1.07	No description of literature search method or sources given. In all studies included in this meta-analysis FP is given at half or less than half the mcg dose as the other ICS. FP given over a dose range of 200-800mcg/day was more effective in terms of improvement in PEFR and less likely to suppress mean morning serum cortisol levels than BUD given over a range of 400-1600mcg/day.

								FP over 200-1000mcg/day was equally effective and causes a similar degree of adrenal suppression as BDP 400-2000mcg/day. In studies at higher doses of ICS, FP was associated with a superior profile in terms of adrenal suppression, than in the lower dose studies.
Connolly[2]	1995	Open, randomised, parallel group study	+	Adult age 18–70 (mean =40) yrs, FEV_1 >= 50% pred. Mean PEFR =79% pred. 77% on no ICS, all using =< 200mcg/day ICS. >= 15% diurnal or b2-agonist induced PEFR variability Randomised to 8 weeks treatment either FP 100 mcg bd via D (n=98) or BUD 200 mcg bd via RPD (n=91).	Improvement in am PEFR Improvement in % of symptom free days and nights Improvement in number of days / nights not using beta2-agonist Mean serum am cortisol levels	FP = 39.7 l/min BUD = 26.1 l/min FP =24% extra days and 29% extra nights BUD = 0 extra days and 17% extra nights Approx. I extra beta2-agonist free day and night in group using FP cf to BUD FP = 437 nmol/l BUD = 441 nmol/l	ns p=0.05 p=0.01 ns	FP 200 mcg/day compared to BUD 400 mcg/day. At a dose of FP at half that of BUD, there was a similar improvement in morning PEFR between the 2 groups, but FP was associated with a superior improvement in asthma symptoms and beta2-agonist requirements. Neither treatment caused a significant suppression of serum cortisol. Expression of some results is poor, with the

								actual reduction in beta2-agonist dosage and number of days/nights that were symptom free not shown
Langdon[3]	1994	Randomised multicentre, open, parallel group study	+	157 patients aged > 16 (mean 46) years FEV_1 >= 50% pred. 15% diurnal or beta2-agonist induced PEFR variability Randomised to 8 weeks treatment either FP 100 mcg bd via MDI (n=81) or BUD 200 mcg bd via MDI (n=76). 20% current smokers included	Improvement in am PEFR Improvements in pm PEFR, FEV_1, FVC, symptom scores, beta2-agonist use Mean serum am cortisol levels	FP = 33 l/min BUD = 25 l/min All improved in both treatment groups, with non-significant improvement in favour of FP in all measurements Increased by 27.9% - FP 18.1% - BUD	p=0.32 ns between groups	FP 200 mcg/day compared to BUD 400 mcg/day In adults 200mcg FP via MDI shown to be equipotent with 400mcg BUD via MDI. Neither treatment caused suppression of adrenocortical function. There was inadequate control of beta2-agonist use prior to clinic measurements of FEV_1, FVC and clinic PEFR .
Langdon[4]	1994	Randomised multicentre, open, parallel group study	+	18-70 yrs old FEV_1 >= 50% pred. 15% diurnal or beta2-agonist induced PEFR variability. On =< 600 mcg ICS/day prior to entry to study	Improvement in am PEFR Improvements in pm PEFR, FEV_1, FVC, symptom scores, beta2-agonist use Mean serum am cortisol	FP = 46 l/min BUD = 27.1 l/min All improved in both treatment groups, with non-significant improvement in favour of FP in all measurements	p < 0.01 ns between groups	FP 400mcg/day compared to BUD 800 mcg/day In adults 400mcg FP via D shown to improve PEFR more than 800mcg BUD via RPD. A more rapid improvement in lung function seen

				Randomised to 8 weeks treatment either FP 200 mcg bd via D (n=139 or BUD 400 mcg bd via RPD (n=136).	levels Oropharyngeal swabs for candidiasis	Unchanged by either treatment FP n=9 BUD n=1	ns between groups	in those patients treated with FP than in those treated with BUD. Neither treatment caused suppression of adrenocortical function. Frequency of clinically suspected and confirmed oropharyngeal candidiasis higher in FP group.
Ferguson[5]	1999	Randomised, double-blind, double-dummy, placebo-controlled parallel group study.	++	Pre-puberty 4-12 yr old, symptomatic asthmatics PEFR =< 85% pred. with >= 15% beta2-agonist induced PEFR reversibility On baseline ICS 400-800mcg/day BDP/BUD or 200-400 mcg/day FP. Randomised to 20/52 400mcg FP via D (n=166) or 800mcg BUD via T (n=167)	Improvement in am PEFR Improvement in day and night time symptom score, rescue therapy use, FEV_1 and FVC Mean morning serum cortisol concentration Mean increase in linear height	FP = 35 l/min BUD = 23 l/min All improved in both treatment groups, with no significant differences between groups FP=199nmol/l BUD=183nmol/l FP= 33.1mm, BUD = 19.9mm	p = 0.002 ns between groups ns between groups p = 0.002	FP 400 mcg/day compared to BUD 800 mcg/day Over the 20 week study, half the dose of FP compared to BUD caused a superior improvement in morning PEFR and was equally effective in improving symptoms and rescue therapy use. Safety was carefully assessed in this study with adverse events, blood tests, hepatic and renal function all being assessed as well

								as height and serum cortisol levels. In a subgroup of patients in whom height had been assessed by stadiometry, (N=76 FP, N=78 BUD) linear growth over 20 weeks was superior in those children treated with FP. Neither treatment caused significant suppression of cortisol secretion. Oropharyngeal candidiasis was not seen.
Basran6	1997	Open, block randomised, parallel group study.	+	18-60 yr old asthmatics, FEV_1 >= 40% pred., still symptomatic despite 400-800mcg ICS at baseline. Randomised to 8 weeks treatment at half baseline dose, either 200 or 400mcg FP via D (n=92) or 200 or 400mcg BUD via T (n=79)	am PEF pm PEF FEV_1/FVC Asthma symptoms beta2-agonist use Oral candidiasis swabs	No difference between groups for any parameter measured	p>0.05	Equal doses of FP and BUD 200-400 mcg/day compared. Despite fact that patients randomised to a dose of FP or BUD at half the dose of ICS that they had been taking prior to the trial, there was no deterioration in asthma control seen in either group. Therefore no difference in efficacy detected between FP and BUD. Little safety data

								collected in this trial except reported adverse events and oral candida swabs.
Hoekx[7]	1996	Randomised, double-blind, double-dummy, parallel group study	++	229 children still symptomatic or with 15% reversibility to beta2-agonists despite 200-400mcg/day ICS at baseline. Randomised to 8 weeks treatment either FP 400 mcg/day via D (n=119) or BUD 400 mcg/day via T (n=110) Baseline PEFR close to 100% for both groups	am PEFR pm PEFR Improvement in activity scores Morning serum cortisol nmol/l Blood and urine markers of bone formation and resorption	FP vs BUD 274 vs 267 279 vs 273 by FP vs BUD 291 vs 246 All parameters remain within normal range	p=0.019 p=0.054 p=0.03 p=0.074 ns	Equal doses of FP and BUD 400 mcg/day compared 25% of patients recruited into this study did not have sufficient symptoms to meet entry criteria. PEFR close to 100% predicted in both groups at baseline, making differences in efficacy difficult to detect. Minimal improvement in PEF and asthma symptom scores and activity levels seen in favour of FP. No evidence of suppression of adrenocortical activity seen at these doses. No consistent evidence of effect on bone metabolism seen for either treatment.
Venables[8]	1996	Randomised, open, parallel	+	Adult age 18–70 (mean =40) yrs,	increase in am PEFR from baseline	FP bd =32l/min BUD od =32l/min	p<0.0001 vs baseline all groups.	Equal doses of FP and BUD 400 mcg/day

		group study. 3 treatment groups compared		PEFR >= 60% pred. (mean =76% pred.) using =< 200mcg/day ICS. All had symptoms >= 3 days/week and/or used b2-agonists >= x 1 per day (mean = 3.7 puffs/24h) Randomised to 8 weeks treatment either FP 200 mcg bd via D (n=74) or BUD 400 mcg nocte via T (n=77) or BUD 200 mcg bd via T (n=79). 4 week cross-over phase to assess preference to T or D.	pm PERF, symptom scores, beta2-agonist use, sleep disturbance, FEV_1/FVC Patient preference No safety data collected, except adverse events	BUD bd =21l/min No difference between groups Turbohaler found to be easier to teach to use, understand and preferred by approx. 55%	No difference between groups p=0.012	compared – Two regimes of BUD at same dose compared > 70 % of these patients were not on ICS prior to initiation of trial.

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