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Ciclesonide

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Contents

Abstract

▲ Ciclesonide is an inhaled corticosteroid (delivered via a hydrofluoroalkane metered-dose inhaler) that is converted to an active metabolite, desisobutyryl-ciclesonide, in the lung, thereby minimising effects on endogenous cortisol.

▲ In two 12-week, randomised studies in patients with asthma, ciclesonide 80 or 320μg once daily was at least as effective as budesonide 400 μg/day at increasing forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) from baseline; ciclesonide 320μg daily was significantly more effective than budesonide 400μg once daily in one study.

▲ In a randomised, double-blind study in patients with asthma controlled with high-dosages of inhaled corticosteroids, FEV_1 and FVC decreased significantly from baseline at 12 weeks in patients receiving ciclesonide 320μg daily or budesonide 400μg daily; peak expiratory flow values decreased significantly only in patients receiving budesonide.

▲ Inhaled ciclesonide 80 or 320μg daily improved asthma symptom scores and decreased the use of rescue medication by a similar, significant amount to budesonide 400 μg/day in two 12-week studies.

▲ Inhaled ciclesonide was generally well tolerated in patients with asthma. Ciclesonide did not suppress biochemical markers of adrenal function in 52-week studies. The long-term (>52 weeks) systemic effects of ciclesonide remain unknown.

Features and properties of ciclesonide (Alvesco®)	
Indication	
Treatment of asthma	
Mechanism of action	
Inhaled parent compound converted by esterases to desisobutyryl-ciclesonide (des-CIC), a corticosteroid with anti-inflammatory activity	
Dosage and administration (in clinical trials)	
Route of administration	Inhalation via metered-dose inhaler (MDI) containing hydrofluoroalkane (HFA)
Dosage	80–640μg once daily
Pharmacokinetic profile	
Mean lung deposition from HFA-containing MDI	52%
Systemic availability following inhalation (dose 1280μg)	Ciclesonide: 18% Des-CIC: 50%
Metabolism	Ciclesonide: cleavage by esterases to form des-CIC Des-CIC: metabolised by cytochrome P450 enzymes to inactive metabolites
Elimination (dose 6.9mg orally)	Ciclesonide: high first-pass metabolism in liver (>99%); 77.9% of dose recovered in faeces
Elimination half-life	Ciclesonide: 0.71h Des-CIC: 3.5h
Adverse events	
Most frequent	Oropharyngeal (incidence <4%)

Asthma is a chronic inflammatory disease of the airways clinically diagnosed based on symptoms such as wheeze, shortness of breath, chest tightness and cough, and objective evidence of variable airflow obstruction.[1,2] Bronchial hyper-reactivity in asthma is a consequence of the activity of a wide range of mediators and inflammatory cells that can cause remodelling of the airways through fibrosis and smooth muscle proliferation.[2-6] The incidence of diagnosed asthma is reported to be about 5% in those aged between 20 and 44 years[7] and about 11% in children.[8] The aetiology of asthma is not fully understood,[2,8] but is likely to involve both genetic and environmental components.[2]

Inhaled corticosteroids currently have a central role in the treatment of asthma,[1,2,4-6,9-13] and have been shown to improve lung function[2,3,10,12,14] and reduce symptoms,[2,3,12,14] exacerbations,[2,10,12,14] hospital readmissions and mortality caused by asthma,[2] and reduce the use of oral steroids in patients with severe disease.[12] They are recommended for patients with asthma using an inhaled β_2-agonist more than once a day, and in patients with recent exacerbations, nocturnal asthma or impaired lung function.[1,2] Low doses of inhaled corticosteroids (<800 μg/day in adults or <400 μg/day in children of beclometasone dipropionate or equivalent) can impart short-term adverse effects, such as dysphonia and oral candidiasis.[1] Long-term, high doses of inhaled corticosteroids may be associated with reduced bone mineral density, cataracts, glaucoma, hypothalamic-pituitary-adrenal-axis suppression and a decrease in growth velocity in children.[1-3] New corticosteroids that are active in the lung but are inactivated when they reach the systemic circulation continue to be researched and produced.[4]

This profile focuses on the potential role of ciclesonide (Alvesco®[1]), a new inhaled corticosteroid in the treatment of patients with asthma. The ciclesonide 100μg metered-dose inhaler (MDI) delivers 80μg ciclesonide per actuation; this review refers to the delivered dose via an MDI unless otherwise stated.

1. Pharmacodynamic Profile

Inhaled ciclesonide is the parent compound that is converted to the active metabolite desisobutyryl-ciclesonide (des-CIC).[15] Des-CIC, previously named ciclesonide active principle (CIC-AP), B-9207-021 and R-M1, is a corticosteroid with anti-inflammatory activity.[11,16-23] Corticosteroids are understood to exert their anti-inflammatory effects in asthma by inhibiting inflammatory and immunological cell activity, the synthesis of proinflammatory cytokines and by affecting adhesion molecule expression, cellular trafficking and function, as reviewed in detail in previous publications.[4,13]

- *In vitro* studies have confirmed that ciclesonide is the inactive parent compound of the active metabolite des-CIC, that the 16-(*R*)-epimer of ciclesonide confers greater anti-inflammatory activity than the 16-(*S*)-epimer of ciclesonide, and that the anti-inflammatory activity of des-CIC is similar to that of other corticosteroids used in the treatment of asthma.[11,17,19-24] Des-CIC inhibits the proliferation of inflammatory cells and the release of inflammatory mediators, including tumour necrosis factor-α, interleukin (IL)-4 and IL-5, *in vitro*.[20,22,23] Ciclesonide also has beneficial effects in animal models of inflammatory airways disease.[19,21-23,25]

Pulmonary Effects

- Ciclesonide attenuated both early- and late-phase allergen-induced bronchoconstriction in patients with mild allergic asthma in a 7-day randomised, double-blind, crossover study.[5] The effect of inhaled ciclesonide 800μg administered twice daily as powdered capsules via a Cyclohaler™ (respirable fraction 21–32% at flow rate used) on early (EAR) and late allergic reactions (LAR) was examined by measuring forced expiratory volume in 1 second (FEV_1) following allergen challenge.[5] The reduction in FEV_1 following allergen challenge was significantly greater in patients treated with placebo than in those treated with ciclesonide (EAR 0.43 vs 0.23L; LAR 0.44 vs 0.21L; both $p < 0.05$).[5]

1 Use of brand names is for product identification purposes only and does not imply endorsement.

• Inhaled ciclesonide also attenuated airway responsiveness to adenosine monophosphate (AMP) in patients with mild-to-moderate asthma in three studies.[10,14,26] In a randomised, double-blind, placebo-controlled, crossover study in 29 patients,[10] dose-related improvements in airway responsiveness (as measured using the provocative concentration of AMP causing a 20% fall in FEV_1 [$PC_{20}FEV_1$]) were seen with ciclesonide 200 and 800μg twice daily administered via a Cyclohaler™ ($p < 0.05$ vs placebo); there was no significant difference between ciclesonide 50μg twice daily and placebo.[10] Patients receiving ciclesonide 200 or 800μg also showed reduced sputum eosinophil levels.[10]

• In the two other studies of airway hyper-responsiveness, inhaled ciclesonide 320–1280 μg/day was as effective at reducing airway responsiveness as fluticasone propionate 1000–2000 μg/day (metered dose)[26] and budesonide 400 μg/day administered via a Turbuhaler® device.[14]

• Measurement of morning peak expiratory flow (PEF) in an 8-week study in 209 patients with mild-to-moderate asthma suggested that once-daily administration of ciclesonide in the evening may be more effective than administration in the morning.[9] In this randomised, double-blind study, patients receiving ciclesonide 160μg in the evening showed significantly greater improvements from baseline in morning PEF than patients receiving the same dosage in the morning (30 vs 3 L/min; $p < 0.05$).[9] Only patients receiving evening administration showed significant improvements from baseline in evening PEF (16 L/min; $p < 0.05$).[9] However, no between-group differences were reported for FEV_1, forced vital capacity (FVC) and asthma symptom scores, all of which improved significantly from baseline in both treatment arms.[9]

• Ciclesonide 320 and 640μg twice daily showed similar efficacy in a 12-week, double-blind, randomised trial in 365 patients with moderate-to-severe asthma.[27] Both dosages significantly improved PEF and FEV_1 from baseline (both $p < 0.05$);[27,28] the improvement in FEV_1 was sustained during a 40-week open-label extension phase.[28]

• The results of studies comparing the effect of ciclesonide on lung function with placebo[29-31] and budesonide[15,32,33] are presented in section 3.

Systemic Glucocorticoid Effects

• Inhaled ciclesonide does not appear to suppress endogenous cortisol release. Several short-term (≤8 weeks) studies using inhaled ciclesonide at dosages of 200–1600 μg/day (metered dose) in healthy volunteers[6,34] or patients with mild-to-moderate asthma[5,9,10,35] showed no significant decrease from baseline in serum levels or urinary excretion of cortisol. Furthermore, inhaled ciclesonide had a minimal effect on adrenal function in a pooled analysis of ten studies in healthy volunteers and patients with asthma, at dosages of 320–2880 μg/day.[11]

• Two randomised, double-blind studies have shown that inhaled ciclesonide has significantly less effect on cortisol production than fluticasone propionate.[26,36] Patients with asthma receiving fluticasone propionate 880–2000 μg/day showed significantly reduced plasma and urinary cortisol levels[26] and low-dose (1μg) tetracosactide peak stimulated serum cortisol levels[36] compared with patients receiving ciclesonide 320–1280 μg/day after 1 (n = 26; crossover study)[26] or 12 (n = 164)[36] weeks' treatment.

• In the therapeutic studies presented in section 3, where stated, ciclesonide did not suppress endogenous cortisol production, as measured by serum cortisol or 24-hour urinary cortisol levels.[15,31,33]

• The administration of high doses of inhaled corticosteroids may have systemic effects, such as a reduction in markers of bone formation, for example bone-specific serum alkaline phosphatase and osteocalcin.[13] However, ciclesonide appears to lack these detrimental effects.[27,28] Significant increases from baseline in serum osteocalcin levels were observed at 12[27] and 52[28] weeks, and raised bone-specific alkaline phosphatase levels were seen at 52 weeks[28] (all $p < 0.05$; quantitative data not reported) in patients with moderate-to-severe asthma receiving ciclesonide 320 or 640μg inhaled twice daily for 12 weeks, followed by an individualised dose of ciclesonide for up to 40 weeks.

2. Pharmacokinetic Profile

The pharmacokinetic profile of inhaled ciclesonide (administered using a hydrofluoroalkane [HFA]-containing MDI, unless stated otherwise) and its active metabolite des-CIC has been evaluated in adult healthy volunteers[11,34,37-40] and patients with asthma.[11,16,38] Additional data from *in vitro* studies have been included where data are limited.[18] With the exception of two fully published studies,[11,18] all data are available as abstracts. Notably, there was no difference in the pharmacokinetic profile of ciclesonide in patients with asthma to that in healthy volunteers, indicating that the presence of asthma did not affect airway distribution or penetration by aerosolised ciclesonide.[38] The pharmacokinetics of ciclesonide and des-CIC are briefly described below.

- The mean lung deposition of inhaled ciclesonide was 52% of the delivered dose in a trial in 8 healthy volunteers; the mean deposition on the mouth/pharynx was 38%.[39,40]
- Compared with values obtained after intravenous administration of ciclesonide 800μg to 12 healthy volunteers in a randomised, crossover study, the mean absolute bioavailability of ciclesonide following a single inhaled dose of 1280μg was 18%.[34] The mean systemic availability of des-CIC was 50%.[34]
- Ciclesonide is highly protein bound in the plasma, with a free fraction of <1%,[17] and does not accumulate in red blood cells.[37] Des-CIC has a volume of distribution of 1190L.[11]
- *In vitro* data show that the biotransformation of ciclesonide to des-CIC is catalysed by esterases and, upon exit from the lung, des-CIC undergoes rapid hepatic metabolism by cytochrome P450 (CYP) enzymes, especially the CYP3A4 isoenzyme,[18] to inactive metabolites.[11]
- Ciclesonide has almost complete first-pass metabolism following oral administration, resulting in a systemic oral bioavailability of des-CIC of <1%.[37] In a study in six healthy volunteers given oral radiolabelled [^{14}C]ciclesonide 6.9mg, ciclesonide was undetectable in subsequent serum samples, and des-CIC was nearly undetectable (<25 ng/L).[37] With regards to activation of parent compound deposited in the oropharynx, a study in 18 asthmatic patients has shown that oropharyngeal enzymatic cleavage of ciclesonide to form des-CIC is limited.[16]
- Ciclesonide is rapidly eliminated; pooled data indicate that the elimination half-life of ciclesonide is 0.71 hours and that of des-CIC, 3.5 hours.[17] In a single-dose, crossover study in healthy volunteers, 77.9% and 66.0% of total radioactivity after oral (6.9mg) and intravenous (0.64mg) doses of radiolabelled [^{14}C]ciclesonide was recovered in the faeces.[37] Drug recovery was complete 120 hours after administration.[37]

3. Therapeutic Efficacy

The efficacy of ciclesonide in the treatment of adult patients with asthma has been studied in five 12-week, randomised, double-blind trials available as abstracts/posters.[15,29,30,32,33] Patients with mild-to-severe asthma were enrolled in one trial;[33] the severity of asthma was not stated in the other four.[15,29,30,32]

Ciclesonide was compared with placebo in two of the trials[29,30] (one of which had a 40-week open-label extension phase[31]) and with budesonide (administered via a Turbuhaler® device) in the other three;[15,32,33] one trial was double-blind with respect to two different dosages of ciclesonide but open-label for budesonide.[15] Where stated, inhaled ciclesonide was administered via an HFA-containing MDI[15,32,33] once daily in the morning[15,29,30,32] or in the evening.[33]

Four of the trials had similar inclusion criteria. Patients were randomised if, during the 2-week baseline period, they had an objective measurement of decreased lung function: FEV_1 values of 50–90% (while receiving rescue medication only)[15,33] or 60–90% (while receiving pretreatment with inhaled beclometasone dipropionate 400–800 μg/day or equivalent)[29,30] of the predicted value. In the other study,[32] patients received pretreatment with beclometasone dipropionate 400–800 μg/day or equivalent for 2 weeks followed by budesonide 1600 μg/day for 2–4 weeks. Patients who demonstrated an increase in FEV_1 of ≥7% or 150mL after

treatment with high-dose budesonide were subsequently randomised to study medication.[32] Patients were also required to exhibit reversible bronchial obstruction in four trials.[29,30,32,33]

The primary endpoints in the placebo-controlled studies were PEF and lack-of-efficacy (asthma exacerbation),[29,30] and in comparative studies with budesonide, improvement in FEV_1.[15,32,33] Secondary endpoints included FVC, PEF and asthma symptom score,[15,32,33] and FEV_1.[31] Where stated, PEF was measured by the patient and recorded in a diary[15,32,33] along with asthma symptom score and the use of rescue medication.[33]

Placebo-Controlled Studies

- After 12 weeks' treatment, ciclesonide maintained or slightly increased PEF from corticosteroid pretreated baseline values; in both studies, ciclesonide recipients had significantly better PEF values than those receiving placebo.[29,30] In one study at week 12, PEF decreased from baseline in placebo recipients but increased from baseline in patients receiving ciclesonide 80 μg/day ($p = 0.0012$ vs placebo) or 320 μg/day ($p = 0.0006$ vs placebo) [figure 1].[29] In the other study, PEF remained stable in patients receiving ciclesonide 160μg (n = 107) or 640μg (n = 112) daily (values not stated), but decreased by 28 L/min in patients receiving placebo (n = 110) [both $p < 0.0001$ vs placebo].[30]
- Patients receiving ciclesonide were more likely to complete the two studies without meeting lack-of-efficacy criteria than patients receiving placebo.[29,30] Less than half of the patients receiving placebo completed the studies without meeting lack-of-efficacy criteria (37%[30] and 45%[29]), whereas more than 60% of patients receiving ciclesonide did so (62–77%[29,30]). The difference in this endpoint for both dosages of ciclesonide (160 and 640μg daily) was significant compared with placebo in one study ($p < 0.0001$);[30] in the other study, significantly more patients receiving ciclesonide 320μg daily completed the study than those receiving a dose of 80μg daily (77% vs 62%; $p < 0.0001$).[29]
- Inhaled ciclesonide maintained or increased FEV_1 from baseline values in both trials.[29,30] In one study, FEV_1 increased by 129 and 192mL in patients receiving ciclesonide 80 μg/day ($p = 0.0044$ vs placebo) or 320 μg/day ($p = 0.0001$ vs placebo) compared with baseline, but decreased by 28mL in patients receiving placebo (figure 1).[29] In the other study, FEV_1 remained stable in patients receiving ciclesonide 160 or 640μg daily (values not stated) but decreased by 144mL in placebo recipients (both $p \leq 0.01$ vs placebo) compared with baseline.[30]
- In an open-label extension[31] of one of these trials,[30] patients completing the double-blind phase (n = 283) received ciclesonide ≥640 μg/day for 4 weeks followed by an individualised dose of ciclesonide for ≤40 weeks. FEV_1 significantly improved during the extension phase (quantitative data not reported in abstract) irrespective of whether patients had received ciclesonide 160 μg/day ($p = 0.0133$), ciclesonide 640 μg/day ($p = 0.0003$) or

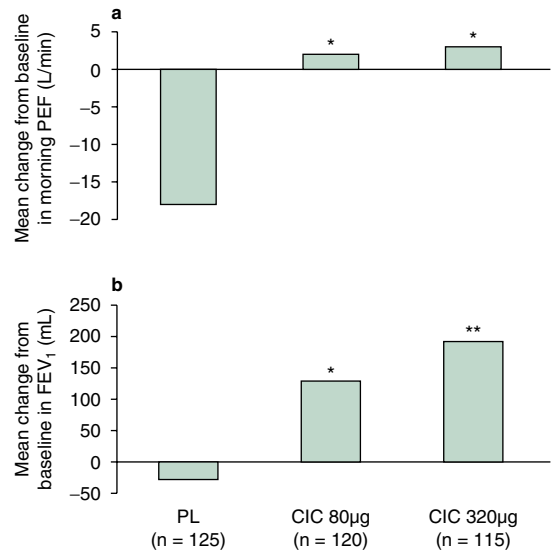

Fig. 1. Effect of inhaled ciclesonide (CIC) on lung function in patients with asthma. Mean change from baseline at endpoint (12 weeks) in (**a**) morning PEF and (**b**) FEV_1 in 360 patients receiving placebo (PL), CIC 80 or 320μg in a randomised, double-blind, multicentre study.[29] All study treatments were administered once daily in the morning via a metered-dose inhaler. Patients were treated in the baseline period with inhaled beclometasone dipropionate 400–800 μg/day or equivalent for 2 weeks prior to randomisation. Severity of asthma was not reported in the abstract. **FEV_1** = forced expiratory volume in 1 second; **PEF** = peak expiratory flow; * $p < 0.005$, ** $p = 0.0001$ vs PL.

placebo (p = 0.0001) during the initial double-blind phase of the trial.[31]

Comparisons with Budesonide

- Inhaled ciclesonide was more effective than once-daily budesonide, and as effective as twice-daily budesonide, at increasing FEV_1 values from baseline, prior to which patients received rescue-medication only, in two 12-week trials.[15,33] In one study (figure 2), patients receiving ciclesonide 320μg daily (n = 198) showed a significantly greater increase in mean FEV_1 from baseline compared with those receiving budesonide 400μg once daily (n = 201) [416mL vs 321mL; p < 0.02].[33]
- In the other study, predicted FEV_1 increased by 9%, 8% and 10% in patients receiving ciclesonide 80μg (n = 182) or 320μg (n = 195) daily or budesonide 200μg twice daily (n = 177), respectively (all p < 0.0001 vs baseline); no significant differences were reported between groups.[15] Mean FEV_1 values in these two trials at baseline ranged from 2.32 to 2.51L.[15,33]

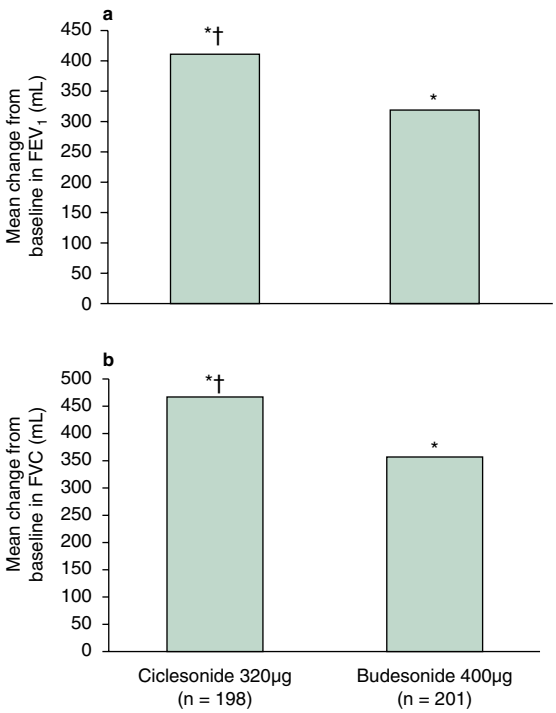

Fig. 2. Effect of inhaled ciclesonide on lung function in patients with mild-to-severe asthma. Mean change from baseline at endpoint (12 weeks) in (**a**) FEV_1 and (**b**) FVC in 399 patients receiving ciclesonide 320μg via a metered-dose inhaler or budesonide 400μg via a Turbuhaler® in a randomised, double-blind, multicentre study.[33] Both study treatments were administered once daily in the evening. **FEV_1** = forced expiratory volume in 1 second; **FVC** = forced vital capacity; * p < 0.0001 vs baseline; † p < 0.05 vs budesonide.

- Inhaled ciclesonide was more effective than once-daily budesonide, and as effective as twice-daily budesonide, at increasing FVC values from baseline in these trials.[15,33] A significantly greater improvement from baseline in FVC was seen in patients receiving ciclesonide 320μg once daily compared with those receiving budesonide 400μg once daily (455 vs 352mL; p = 0.03) [figure 2].[33] In the other study, FVC values increased significantly from baseline in all three treatment arms (quantitative data not reported; p < 0.0001).[15]
- Furthermore, these trials demonstrated that inhaled ciclesonide (at dosages of 80 or 320μg once daily) improved morning and evening PEF from baseline to a similar extent to budesonide (at dosages of 400μg once daily or 200μg twice daily), and no between-group differences were reported (quantitative data not documented);[15,33] in one trial, these changes were significant from baseline (p < 0.0001).[33] In the latter trial, morning PEF indicated an earlier onset of treatment effect with ciclesonide (day 3) than with budesonide (week 2).[33] Mean PEF values at baseline, reported in only one trial, ranged from 352 to 365 L/min.[33]
- At 12 weeks, comparable, significant (p < 0.0001) improvements from baseline in asthma symptom scores and use of rescue medication were seen in both treatment groups in these two trials comparing ciclesonide with budesonide.[15,33]
- In a third study in which patients were pretreated with inhaled budesonide 1600μg daily for 2–4 weeks and subsequently randomised to receive ciclesonide 320μg (n = 179) or budesonide 400μg (n = 180) once daily for 12 weeks, both groups showed decreases in FEV_1 values from baseline (−178mL vs −232mL; both p < 0.0001 vs baseline), with no significant difference reported between groups (figure 3).[32] Mean FEV_1 values at baseline were 2.61 and 2.44L.[32]

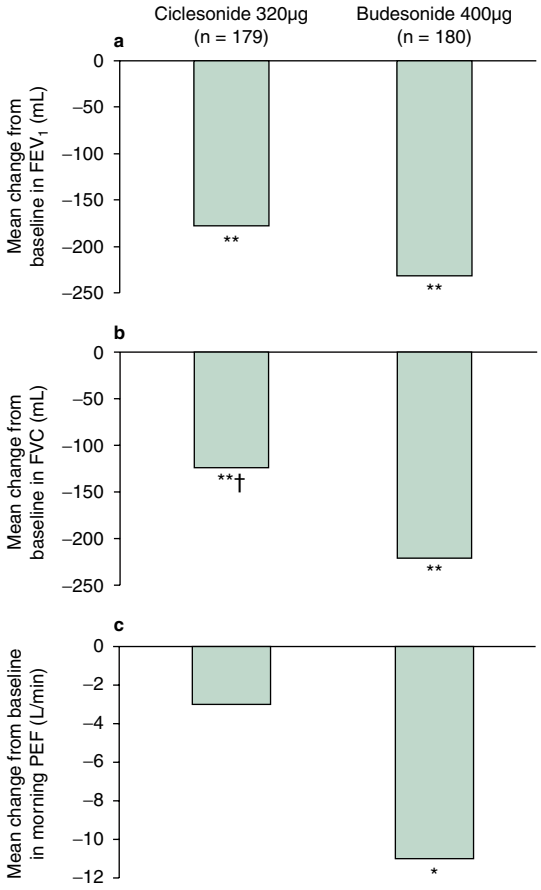

Fig. 3. Effect of inhaled ciclesonide on lung function in patients with asthma. Mean change from baseline at endpoint (12 weeks) in (**a**) FEV_1, (**b**) FVC and (**c**) morning PEF in 359 patients receiving ciclesonide 320µg via a metered-dose inhaler or budesonide 400µg via a Turbuhaler® in a randomised, double-blind, multicentre study.[32] Both study treatments were administered once daily in the morning. Patients were pretreated with inhaled beclometasone dipropionate 400–800 µg/day or equivalent for 2 weeks followed by budesonide 1600 µg/day for 2–4 weeks prior to randomisation. Severity of asthma was not reported in abstract. **FEV_1** = forced expiratory volume in 1 second; **FVC** = forced vital capacity; **PEF** = peak expiratory flow; * $p < 0.01$, ** $p \leq 0.0001$ vs baseline; † $p < 0.01$ vs budesonide.

● In this trial, a significantly smaller decrease in FVC from baseline was seen in patients randomised to ciclesonide than in budesonide recipients (−124 vs −221mL; $p < 0.01$) [figure 3].[32] Furthermore, patients randomised to ciclesonide showed a non-significant decrease in morning PEF from baseline (−3 L/min), whereas in those treated with budesonide this decrease was significant (−11 L/min; $p < 0.01$) [figure 3].[32] However, the difference between groups was not significant.[32]

● At 12 weeks, a similar change from baseline in asthma symptom score was seen in both treatment arms; however, a significantly higher number of symptom-free days was seen in patients receiving ciclesonide than in budesonide recipients (43% vs 34%; $p = 0.03$).[32] The median use of rescue medication was significantly lower in patients receiving ciclesonide than in those receiving budesonide ($p < 0.05$); however, the number of rescue medication-free days was similar in both groups.[32] A similar number of patients in this trial suffered exacerbations due to lack of efficacy in the ciclesonide and budesonide groups (14% vs 19%).[32]

4. Tolerability

Ciclesonide was generally well tolerated in patients with asthma in the clinical trials presented in section 3. However, only limited tolerability data are available in these abstracts/posters.

● No significant differences in the number of adverse events between treatment arms in the 12-week trials comparing ciclesonide with budesonide were reported.[15,32,33] The incidence of adverse events, reported in two trials only, was 28%[33] and 41.9%[32] in patients receiving ciclesonide 320µg daily and 27%[33] and 51.7%[32] in those receiving budesonide 400µg daily; the higher frequency in both treatment arms occurred in patients pretreated with inhaled budesonide 1600 µg/day for 2–4 weeks prior to randomisation.[32]

● In a 40-week, open-label extension study, during which 283 patients were treated with an individualised dose of inhaled ciclesonide after randomisation to ciclesonide 160 or 640µg daily or placebo for 12 weeks followed by ciclesonide ≥640 µg/day for 4 weeks, 10 patients (3.5%) reported oropharyngeal adverse effects,[31] a common adverse effect of inhaled corticosteroids reported in ≤5% of adult patients.[13] However, no cases of oropharyngeal adverse events were reported in any of the other studies.[15,29,30,32,33] Where documented, no laboratory abnormalities occurred during treatment with in-

haled ciclesonide at dosages ranging from 320 to ≥640 μg/day in 12-[33] and 52-week trials.[31]

- The effect of ciclesonide on serum and urinary cortisol levels and other markers of systemic glucocorticoid activity are presented in section 1. The long-term (>52 weeks) systemic effects of inhaled ciclesonide have not been determined.

5. Dosage and Administration

Formal recommendations for the administration of ciclesonide to patients with asthma are not available. However, in clinical trials, ciclesonide was administered once daily via an HFA-containing MDI. Dosages of ciclesonide shown to have a beneficial effect on lung function and to improve asthma symptoms in patients with mild-to-severe asthma ranged from 80 to 640μg daily.

6. Ciclesonide: Current Status

Ciclesonide, administered via an HFA-containing MDI, is currently in preregistration for the treatment of asthma in several countries worldwide, including North America, Europe and Australia.[41] It has shown clinical efficacy in five well-designed trials in this indication and was generally well tolerated. In these trials, ciclesonide did not suppress endogenous cortisol release, and oropharyngeal adverse effects, reported in one trial only, had a similar incidence to that generally observed with inhaled corticosteroids.

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