The Inhaled Steroid Treatment As Regular Therapy in Early Asthma (START) study 5-year follow-up: Effectiveness of early intervention with budesonide in mild persistent asthma

William W. Busse, MD,[a] Søren Pedersen, MD,[b] Romain A. Pauwels, MD,[c,†] Wan C. Tan, MD,[d] Yu-Zhi Chen, MD,[e] Carl Johan Lamm, PhD,[f] and Paul M. O'Byrne, MD,[g] on behalf of the START Investigators Group *Madison, Wis, Kolding, Denmark, Ghent, Belgium, Queenstown, Singapore, Vancouver, British Columbia, Canada, Beijing, China, Lund, Sweden, and Hamilton, Ontario, Canada*

Background: The Inhaled Steroid Treatment as Regular Therapy in Early Asthma (START) study enrolled 7241 patients aged 5 to 66 years with recent-onset, mild persistent asthma to assess early intervention with the inhaled corticosteroid budesonide on long-term asthma control.

Objective: The open-label phase of the START study was included to determine the effect on lung function and asthma control of adding budesonide to the reference group patients who had not initially received inhaled corticosteroids.

Methods: Patients were randomized to double-blind treatment with budesonide, 200 μg (those aged <11 years) or 400 μg once daily, or placebo plus the usual asthma therapy for 3 years, after which all patients received 2 years of open-label treatment with budesonide once daily.

Results: During the full 5-year study period, postbronchodilator FEV_1 percent predicted decreased, irrespective of randomized treatment during the double-blind phase, by an average of 2.22% (SE, 0.15%). However, patients with inhaled budesonide in the double-blind phase had a significantly lower risk (odds ratio, 0.61; $P < .001$) of a severe asthma-related event during the full 5-year study period than those in the reference group. Moreover, patients in the reference group used more additional asthma medications during both the open-label and double-blind phases.

Conclusions: In mild persistent asthma early intervention with inhaled budesonide was associated with improved asthma control and less additional asthma medication use. (J Allergy Clin Immunol 2008;121:1167-74.)

Key words: *Mild persistent asthma, recent-onset asthma, budesonide dry-powder inhaler, inhaled corticosteroid*

Asthmatic patients with mild persistent disease can experience considerable asthma-related morbidity[1-4] and even mortality.[5,6] Guidelines recommend inhaled corticosteroids (ICSs) as the preferred initial choice of anti-inflammatory therapy in patients with persistent asthma[7,8] based on gain of greater asthma control (ie, reduced current impairments), decreased exacerbations (diminishing future risks), and improved quality of life.[2,3] Previous studies have also suggested that early intervention with ICSs in newly diagnosed asthma might reduce other aspects of future risks, including the degree of progressive loss of lung function that can occur in asthma[9] and the influence of the overall treatment response.[10-12] The 5-year Inhaled Steroid Treatment as Regular Therapy in Early Asthma (START) study was designed to determine the potential long-term effectiveness of early intervention with ICSs in adults and children with mild persistent disease of less than 2 years' duration. In the initial phase of this study, patients were randomized to a 3-year double-blind treatment period with either budesonide, 400 μg (200 μg for children aged <11 years) administered once daily through a dry-powder inhaler (Pulmicort Turbuhaler; AstraZeneca Research and Development, Lund, Sweden), or placebo through a Turbuhaler.[1] In addition to the blinded therapy, the managing physician could add other asthma therapy, including the introduction of ICSs to achieve asthma control. This approach to treatment was implemented to ensure asthma control and thus greater patient retention over the duration of the study.[13] The primary outcome variable of the double-blind phase of the START study was the time to the first severe asthma-related event (SARE).[13] In the double-blind phase of the START study, patients who received budesonide had a significant reduction in asthma exacerbations requiring systemic corticosteroids, a longer time to the first SARE, and less of a decrease in prebronchodilator and postbronchodilator FEV_1 values.[1]

This double-blind phase of the START study was followed by 2 years of open-label treatment, during which all patients received budesonide once daily, as well as continuing their usual asthma therapy received to this point. Throughout the study, the use of this additional asthma therapy was recorded. The primary

From [a]the University of Wisconsin Medical School, Madison; [b]the University of Southern Denmark, Kolding Hospital; [c]Ghent University Hospital; [d]the National University of Singapore, Queenstown, and St Paul's Hospital, University of British Columbia, Vancouver; [e]the Capital Institute of Pediatrics, Beijing; [f]AstraZeneca Research and Development, Lund; and [g]McMaster University, Hamilton.

†Deceased.

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Reprint requests: William W. Busse, MD, Department of Medicine, University of Wisconsin School of Medicine and Public Health, J5/219 CSC, Box 2454, 600 Highland Ave, Madison, WI 53792. E-mail: wwb@medicine.wisc.edu.

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Abbreviations used
CAMP: Childhood Asthma Management Program
ICS: Inhaled corticosteroid
OR: Odds ratio
PEAK: Prevention of Early Asthma in Kids
SARE: Severe asthma-related event
START: Inhaled Steroid Treatment As Regular Therapy in Early Asthma

outcome variable of the full 5-year study period was the change from baseline in postbronchodilator percent predicted FEV_1. Secondary outcome variables were the change in prebronchodilator percent predicted FEV_1, the number of SAREs, change in asthma-related symptoms, and use of concomitant asthma medication to achieve asthma control. This article reports the results of the full 5-year study period. Some of the findings have been previously reported in the form of an abstract.

METHODS

Study population

The START study (AstraZeneca Study SD-004-0111) has been described in detail elsewhere.[1,13] Briefly, patients aged 5 to 66 years with recent-onset, mild persistent asthma were enrolled from 499 sites in 32 countries. These patients met the criteria for mild persistent asthma as noted in the US guidelines.[7] Eligible patients had asthma symptoms at least weekly, but not daily, in the 3 months before enrollment. Patients also had reversible airway obstruction, demonstrated by an increase in FEV_1 of greater than 12% after the use of a short-acting β_2-adrenergic agonist, a decrease in FEV_1 of greater than 15% after exercise challenge, or variation of greater than 15% between the 2 highest and 2 lowest peak expiratory flow rates in 14 days. The onset of asthma must have been within 2 years of enrollment, and patients could not have had greater than 30 days of inhaled or oral corticosteroid treatment or more than 1 depot corticosteroid injection per year.[1,13]

Procedures

Patients completing the 3-year double-blind phase of the study were switched to open-label treatment with once-daily budesonide (200 μg for patients aged <11 years at study entry and 400 μg for patients aged ≥11 years at entry study) plus the usual asthma therapy for the final 2 years of the study (Fig 1). Budesonide was given once per day based on evidence that equivalence is seen with daily and twice-daily administration.[14-16] The budesonide group was comprised of those patients who were initially randomized to double-blind treatment with budesonide (years 1–3), and the reference group consisted of those patients who received regular treatment with budesonide only during the open-label phase of the study (years 4 and 5). Patients recorded details of asthma-related events, use of additional asthma medications, asthma symptoms, restrictions in daily activities, and sleep problems caused by asthma between scheduled clinic visits.[13] A SARE was defined as an event requiring hospitalization or emergency treatment because of worsening of asthma or death from asthma. Emergency treatment was defined as treatment of acute airway obstruction with systemic glucocorticosteroids and nebulized or parenteral bronchodilators administered in a health care facility. Follow-up visits were scheduled every 3 months (±14 days) for patient evaluation and data collection.[13] During the study, patients recorded details in a notebook of asthma-related events, as well as asthma control between scheduled visits. These assessments were noted, assessed, and graded by investigators at each scheduled visit. Patients were also asked about use of medications since their last visit, the presence of asthma symptoms, the number of asthma-free days, and the number of days in the previous 2 weeks in which their lives had been restricted by asthma symptoms. Changes in concurrent medications, including inhaled or systemic glucocorticosteroids, could be made if an investigator judged this necessary to achieve asthma control. Serious adverse events were collected from spontaneous reports and by questioning at each clinic visit during the open-label phase of the study.

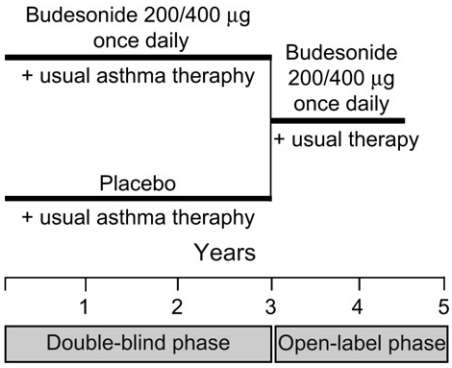

FIG 1. Study design. Patients were randomized to double-blind treatment with inhaled budesonide, 200 μg (aged <11 years) or 400 μg once daily through a Turbuhaler, or placebo plus usual asthma therapy for 3 years. After 3 years, all patients received 2 years of open-label treatment with inhaled budesonide once daily plus usual asthma therapy.

Statistical analysis

The primary efficacy variable for the full 5-year study period was the change from baseline in postbronchodilator FEV_1 percent predicted. Assuming 1800 patients per treatment group and an SD of change from baseline in postbronchodilator FEV_1 percent predicted of 10%, a difference between treatment groups of 1.2% in this variable would be detected with a power of 95% at a significance level (2-sided) of 5%. Change in postbronchodilator and prebronchodilator FEV_1 percent predicted over the full 5-year study period was estimated by using a linear mixed model, including as covariates the randomized treatment, the baseline value, time since the start of the open-label phase, and the interaction between treatment and time. All data assessed in the open-label phase were used, and therefore results are based on both noncompleters and completers of the open-label phase. For comparability with results on lung function in the START study published earlier, all estimates reported in the tables are adjusted to the overall (for all patients in the START study) mean baseline level of postbronchodilator or prebronchodilator FEV_1 percent predicted. The same analysis model was used for all patients (overall) and separately for each age-by-sex stratum and for the stratum of adults (age ≥18 years) ignoring sex.

Treatment groups were compared regarding the risk of having 1 or more SAREs in terms of odds ratios (ORs) unadjusted for time in study. The OR was computed separately for the full study period, the double-blind phase, and the open-label phase, using all patients available in the study or in a certain study phase. SAS version 8.2 (SAS Institute, Inc, Cary, NC) was the software used for statistical analysis.[17]

Role of the funding source

The study was funded through a contract from AstraZeneca Research and Development. The sponsors of the study had no role in the study design, the planning of the data analysis, and the interpretation of the results, with the exception of the company coauthors, who participated in all aspects of the study. The study was performed by the clinical investigators (listed in the Appendix) and monitors, employed by the sponsor, who collected the data. All investigators had free and unlimited access to the raw data and the statistical reports. Staff of the sponsor reviewed the various drafts of the manuscript and made editing suggestions. The authors made final decisions on all aspects of the manuscript.

RESULTS

Study population

In the 2-year open-label phase 5146 patients received regular treatment with budesonide, either as a continuation from the

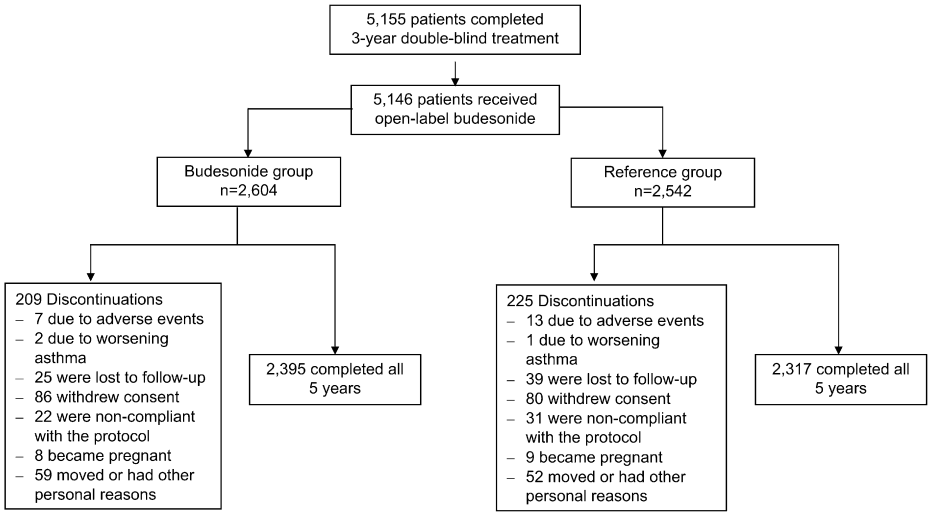

FIG 2. Patient disposition during the 2-year open-label phase of the study. The number of patients who received double-blind treatment was 7221.

TABLE I. Demographic characteristics at baseline (start of the double-blind phase)

	Budesonide (n = 2604)	Reference (n = 2542)
Age-by-sex stratum, n (%)		
5–10 y, female	317 (12.2)	323 (12.7)
Male	497 (19.1)	463 (18.2)
11–17 y, female	209 (8.0)	209 (8.2)
Male	231 (8.9)	202 (8.0)
18-66 y, female	856 (32.9)	808 (31.8)
Male	494 (19.0)	537 (21.1)
Race, n (%)		
White	1629 (62.6)	1612 (63.4)
Black	21 (0.80)	25 (1.0)
Asian	831 (31.9)	792 (31.2)
Other	123 (4.7)	113 (4.4)
Smoking status, n (%)		
Nonsmoker	1359 (52.2)	1281 (50.4)
Passive smoker	778 (29.9)	803 (31.6)
Exsmoker	205 (7.9)	216 (8.5)
Active smoker	262 (10.1)	242 (9.5)

Only patients entered into the open-label phase are shown.

TABLE II. Postbronchodilator percent predicted FEV_1 at baseline (B1)

	Budesonide		Reference	
	BI-1	BI-2	BI-1	BI-2
Overall	96.7 (12.1)	95.0 (12.8)	96.5 (12.3)	93.9 (13.5)
Age-by-sex stratum				
5–10 y, female	97.1 (11.7)	96.0 (12.3)	96.7 (12.7)	95.5 (12.6)
Male	95.5 (12.8)	93.9 (11.4)	95.5 (11.0)	93.2 (12.2)
11–17 y, female	97.8 (12.2)	96.6 (12.4)	96.6 (11.6)	96.5 (11.5)
Male	94.7 (11.6)	95.3 (12.5)	93.6 (11.0)	94.7 (12.4)
18-66 y, female	98.1 (12.1)	96.2 (13.3)	98.0 (12.8)	94.7 (14.7)
Male	95.6 (11.4)	92.4 (13.6)	96.1 (12.6)	91.1 (14.0)

Only patients entered into the open-label phase are shown. Data are presented as means (SD) at BI-1 (ie, the start of the double-blind phase or BI-2 (ie, the start of the open-label phase).

double-blind phase or as an addition during the open-label phase. Of these patients, 2604 had been previously randomized to double-blind treatment with budesonide (budesonide group), and 2542 had been randomized to placebo (reference group; Fig 2). Patient demographics at baseline (start of the double-blind phase) were similar in the budesonide and reference groups (Table I).

For patients entering the open-label phase, retention was higher than 90% in both treatment groups (Fig 2). Few patients in either group discontinued participation because of adverse events or worsening asthma. Most patient discontinuations were due to relocation, personal reasons, withdrawn consent, or loss to follow-up.

Lung function measurements

Both the prebronchodilator and postbronchodilator percent predicted FEV_1 values at baseline were similar in the budesonide and reference groups but differed between age-by-sex strata (Tables II and III). In all age groups mean values of percent predicted FEV_1 were higher in female than in male patients. At the end of the open-label phase, the overall (mean values over all patients) significant differences between treatment groups that existed in postbronchodilator and prebronchodilator percent predicted FEV_1 during the double-blind phase were lost, as shown in Fig 3. However, results in different age-by-sex strata were not homogeneous (Table IV and V).

During the full 5-year study period, the postbronchodilator percent predicted FEV_1 decreased, irrespective of randomized treatment during the double-blind phase ($P = .74$), by an average of 2.22%. However, in adults (age $\geq$18 years), ignoring sex, there was a statistically significant treatment difference of 0.85% ($P = .044$) in favor of budesonide (Table IV).

During the full 5-year study period, prebronchodilator percent predicted FEV_1 increased, irrespective of randomized treatment during the double-blind phase ($P = .20$), by an average of 3.24%. The increase was more pronounced in the pediatric age groups (age <18 years) than in adults. In adults, ignoring sex, a statistically significant treatment difference of 1.21% ($P = .018$) in favor of budesonide was seen between the 2 treatment groups (Table V).

TABLE III. Prebronchodilator percent predicted FEV_1 at baseline

	Budesonide		Reference	
	BI-1	BI-2	BI-1	BI-2
Overall	86.8 (13.4)	90.2 (13.7)	86.4 (13.8)	88.2 (14.3)
Age-by-sex stratum				
5–10 y, female	85.8 (12.6)	91.6 12.5)	86.8 (13.3)	90.3 (13.3)
Male	84.8 (12.7)	88.6 (12.3)	84.6 (11.9)	87.3 (12.8)
11–17 y, female	89.7 (13.5)	92.8 (13.9)	88.4 (13.0)	91.4 (12.6)
Male	85.9 (13.0)	90.5 (12.5)	84.2 (12.1)	89.0 (12.9)
18-66 y, female	88.7 (13.7)	91.7 (14.4)	88.3 (13.7)	89.0 (15.7)
Male	85.3 (13.4)	87.1 (14.6)	86.6 (13.9)	85.2 (14.7)

Only patients entered into the open-label phase are shown. Data are presented as means (SD) at Bl-1 (ie, the start of the double-blind phase) or Bl-2 (ie, the start of the open-label phase).

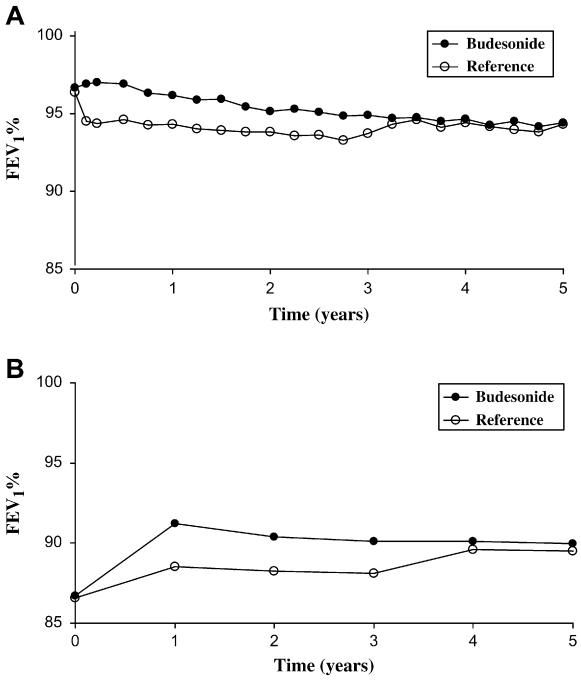

FIG 3. Mean postbronchodilator **(A)** and prebronchodilator **(B)** percent predicted FEV_1 among patients in the budesonide and reference groups completing all 5 years of the study.

In adults, ignoring sex, half the treatment effect of budesonide on lung function (postbronchodilator and prebronchodilator percent predicted FEV_1) remained at the end of the 5-year study period (51% on postbronchodilator FEV_1 percent predicted and 48% on prebronchodilator FEV_1 percent predicted).

SAREs

The incidence rate of SAREs decreased in each group over the 5-year treatment period (Fig 4). During the 3-year double-blind phase, 315 patients (117 in the budesonide group and 198 in the reference group) experienced 1 or more SAREs, with the risk being significantly lower in the budesonide group than in the reference group (OR, 0.57; $P < .001$). Excluding the 315 patients, 30 patients (16 in the budesonide group and 14 in the reference group) experienced 1 or more SAREs during the 2-year open-label phase, with the risk being similar in the 2 treatment groups (OR, 1.12; $P = .76$). The cumulative risk of having 1 or more SAREs during the full 5 years of START was significantly lower in the budesonide group than in the reference group (OR, 0.61; $P < .001$).

TABLE IV. Change in postbronchodilator percent predicted FEV_1 over the study

	Budesonide	Reference	Difference
Overall	−2.17 (0.21)	−2.27 (0.21)	0.10 (0.30), $P = .74$
Age-by-sex stratum			
5–10 y, female	−0.84 (0.57)	0.26 (0.56)	−1.10 (0.80), $P = .17$
Male	−2.28 (0.46)	−1.96 (0.48)	−0.32 (0.66), $P = .63$
11–17 y, female	−1.46 (0.64)	−0.50 (0.63)	−0.95 (0.89), $P = .29$
Male	−0.42 (0.70)	0.51 (0.74)	−0.93 (1.01), $P = .36$
18-66 y, female	−1.89 (0.38)	−3.04 (0.39)	1.15 (0.54), $P = .034$
Male	−4.73 (0.49)	−4.91 (0.47)	0.18 (0.67), $P = .79$
Both sexes	−2.96 (0.30)	−3.81 (0.30)	0.85 (0.42), $P = .044$

Only patients entered into the open-label phase are shown. Data are presented as means (SEs) of the 5-year change estimated by means of mixed model analysis.

TABLE V. Change in prebronchodilator percent predicted FEV_1 over the study

	Budesonide	Reference	Difference
Overall	3.47 (0.25)	3.01 (0.25)	0.46 (0.35), $P = .20$
Age-by-sex stratum			
5–10 y, female	5.21 (0.64)	5.32 (0.64)	−0.12 (0.90), $P = .90$
Male	3.60 (0.52)	4.31 (0.54)	−0.71 (0.75), $P = .35$
11–17 y, female	4.27 (0.79)	4.30 (0.78)	−0.03 (1.10), $P = .98$
Male	4.60 (0.81)	4.92 (0.85)	−0.32 (1.17), $P = .79$
18-66 y, female	3.60 (0.45)	2.32 (0.46)	1.27 (0.64), $P = .046$
Male	0.80 (0.60)	−0.09 (0.58)	0.90 (0.84), $P = .29$
Both sexes	2.57 (0.36)	1.36 (0.36)	1.21 (0.51), $P = .018$

Only patients entered into the open-label phase are shown. Data are presented as means (SEs) of the 5-year change estimated by means of mixed model analysis.

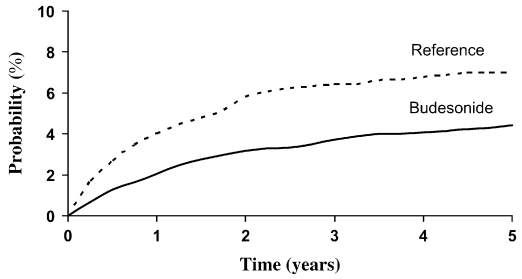

FIG 4. Cumulative probability of having a first SARE. The curves are based on life-table estimates (interval width, 0.25 years) by using all patients entered into the study. The number of patients at risk in the budesonide *(Reference)* group is 3597 (3568) at time 0, 2613 (2486) at time 2.50 years, and 2337 (2195) at time 4.50 years.

Asthma control and use of additional therapy

The reductions in the percentages of patients with symptoms, restrictions in normal activities, and sleep problems caused by asthma from baseline to the end of the double-blind treatment phase were maintained or further improved during the subsequent 2 years of open-label budesonide treatment. Between-group differences, which existed during the double-blind phase, were, however, no longer statistically significant during the open-label

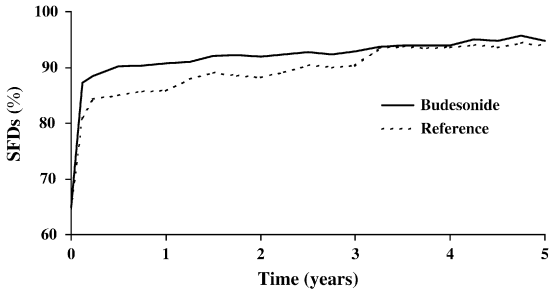

FIG 5. Mean percentage of symptom-free days *(SFDs)* among patients in the budesonide and reference groups completing all 5 years of the study.

phase. The percentage of symptom-free days increased among patients in both treatment groups throughout the 5-year study period (Fig 5), and the differences between groups were no longer significant during the open-label phase.

Patients who received budesonide during the double-blind treatment phase used significantly less additional asthma medication during the open-label treatment phase. Significantly fewer patients in the budesonide group required additional ICSs (10.4% vs 14.6%, $P < .001$), long-acting β_2-adrenergic agonists (6.3% vs 9.3%, $P < .001$), and cromones (0.9% vs 2.1%, $P = .003$) in addition to their budesonide treatment by year 5 (Table VI). Thus to achieve a similar level of control of asthma between the budesonide-treated and reference groups, a greater frequency of amounts of medication was required by the reference group.

Serious adverse events

Budesonide was well tolerated throughout the study, with no new or unexpected safety findings evident at 5 versus 3 years of budesonide treatment. Worsening asthma, accident, fracture, appendicitis, and pneumonia were the most frequently reported serious adverse events during both the double-blind and open-label treatment phases. Fewer serious adverse events and discontinuations caused by adverse events were reported during the 2-year open-label phase compared with during the 3-year double-blind phase.

DISCUSSION

Because of a rapid catch-up in lung function values in the reference group during the open-label phase of the START study, there was no significant overall difference between treatment groups in the 5-year change from baseline, either in the postbronchodilator or prebronchodilator FEV_1 percent predicted values. However, in adults (age $\geq$18 years) nearly half the treatment effect of budesonide on lung function attained in the double-blind phase of the START study still remained at the end of the 5-year study period. This finding in adults is consistent with a number of observational studies that have indicated that a delay in the initiation of ICSs in asthmatic patients is associated with a lower postbronchodilator FEV_1.[18-20] Moreover, some studies also reported this benefit in children.[10,21] The latter was not seen in the present study. The reasons for this difference are not obvious, but the severity of asthma in the children in the study by Agertoft and Pedersen[10] seemed to be somewhat greater than that of the children in the present study.

In the 3-year double-blind phase of the START study, treatment with budesonide significantly improved asthma control, as demonstrated by a reduction in SAREs, breakthrough symptoms, sleep disturbances, and activity limitations.[1] The effects on asthma control in the open-label phase of the START study yielded 3 important findings. First, asthma control, as reflected in features of current impairments, was maintained or improved in patients randomized to early budesonide intervention. Second, the introduction of open-label budesonide after 3 years of usual asthma therapy resulted in a "catch-up" in asthma control in the reference group. Third, a greater proportion of patients in the reference group required significantly more additional asthma medication (ICSs other than budesonide, long-acting β_2-adrenergic agonists, and cromones) to achieve the same level of asthma control during years 4 and 5 of the study.

During both the double-blind and open-label phases of the START study, physicians were instructed to constantly tailor additional asthma medications to achieve clinical control of the disease, which was assessed based on symptoms, medication use, the number of asthma-free days, and the number of days in the previous 2 weeks their lives had been restricted by asthma symptoms. When the use of additional medications was evaluated, it appeared that these instructions were followed. Thus the use of cromones decreased and the use of long-acting β_2-adrenergic agonists increased with time in both treatment groups. Moreover, the use of inhaled and oral corticosteroids was reduced in both groups during open-label treatment. These findings make it unlikely that differences in the use of additional asthma medications between the groups were merely due to a lack of treatment tailoring during the open-label phase.

A diminished response to ICS therapy in the patients with a delayed initiation of budesonide could be another possible explanation for our findings. This has been reported in a previous study, which evaluated the benefit of early versus late intervention with budesonide administered over 5 years in patients with mild or moderate persistent asthma.[22] In this study patients with asthma of less than 2 years' duration had their symptoms controlled on a lower dose of budesonide and used less additional asthma medications, including long-acting β_2-adrenergic agonists, to maintain asthma control than patients with a median asthma duration of more than 5 years before treatment initiation.

The clinical benefits of regular treatment with low-dose ICSs in patients with mild persistent asthma have also been assessed in the Childhood Asthma Management Program (CAMP) study.[23] However, this study was not an early-intervention study because patients in the CAMP study had a mean asthma duration of more than 5 years. The CAMP study treated children from 5 to 12 years of age with low-dose inhaled budesonide, nedocromil, or placebo for at least 4 years. The results from the CAMP study did not demonstrate any difference in the postbronchodilator FEV_1 between treatments but did demonstrate that treatment with ICSs significantly improved airway responsiveness to methacholine, as well as resulting in fewer hospitalizations, fewer urgent visits to a caregiver, fewer courses of prednisone, and a smaller percentage of days on which additional asthma medications were needed. This study is consistent with the results of the START study and suggests an important clinical benefit of low-dose ICSs for patients with mild persistent asthma.

Guilbert et al[24] recently reported on their observations in the Prevention of Early Asthma in Kids (PEAK) study, which was designed to determine whether early introduction of ICSs for

TABLE VI. Percentage of patients using additional asthma medications

	Budesonide (n = 2604)		Reference (n = 2542)		
	Year 4	Year 5	Year 4	Year 5	*P* value*
Inhaled corticosteroids†	11.1	10.4	16.3	14.6	<.001
Oral/systemic corticosteroids	1.5	0.9	1.5	0.7	.79
Short-acting β_2-adrenergic agonists	61.8	60.3	63.8	62.2	.17
Long-acting β_2-adrenergic agonists	5.4	6.3	8.5	9.3	<.001
Xanthines	2.9	2.5	3.3	2.2	1.00
Cromones	1.5	0.9	2.6	2.1	.003
Leukotriene modifiers	1.3	1.4	1.5	1.4	.90
Other	5.2	5.3	5.4	5.2	1.00

Only patients entered into the open-label phase are shown. Data are calculated for the 6 weeks before each time point.
*Budesonide versus reference therapy. *P* values refer to the average percentages for years 4 and 5.
†Includes inhaled corticosteroids other than budesonide, as well as budesonide over the prescribed dose.

2 years would have a sustained effect on asthma control after discontinuation of treatment. In contrast to the START cohort, which had early onset but well-defined characteristics of asthma, the PEAK population was younger, 2 to 3 years of age, and two thirds had 1 or more visits to an emergency department for an asthma exacerbation. The 285 enrolled participants received either placebo or inhaled fluticasone, 88 μg twice daily, for 2 years. After 2 years of treatment, there was no change in the development of asthma symptoms in the following 12-month period. However, during the 2 years of active treatment, inhaled fluticasone reduced the need for systemic corticosteroids for an exacerbation, decreased montelukast use for greater than 2 months, and resulted in less supplemental use of fluticasone. Although the design, objective, and ages of treatment were distinct from the population in the START study, participants in the PEAK study had improved asthma control while taking corticosteroids and, in this sense, parallel the benefits associated with ICS use.

In conclusion, results from the START study support current guideline recommendations for the daily use of ICS therapy in adults and children with mild persistent asthma. The results from the START study also indicate that early intervention with ICSs improves overall treatment effectiveness and reduces the need for additional medication required to maintain asthma control. These findings thus support the recommendations of the recently released "US guidelines for the diagnosis and management of asthma" that ICS use in patients with recent-onset, mild persistent asthma will achieve control of features of current impairment and future risks.[7]

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Clinical implications: Although early intervention with ICSs did not affect lung function, this approach can lead to improved asthma control and result in the need for less additional medication.

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APPENDIX

START Safety Committee

A. Sheffer (Boston, Mass [Chairman]); A. Woolcock (Sydney, Australia); P. Diaz (Santiago, Chile); M. Silverman, (Leicester, United Kingdom); B. Lindmark (Lund, Sweden [nonvoting member]).

START investigators (and numbers of patients recruited) by country

Western and Central Europe

Austria (88)—Josef Eckmayr, Josef Riedler, Gert Wurzinger, Günter Ott, Jasminka Zarkovic, Andrea Schulheim, Manfred Götz, Herwig Schinko, Ingrid Thomüller.

Belgium (223)—Wilfried de Backer, Hugo van Bever, Geert Verleden, Christiane de Boeck, Joseph Aumann, Walter Vincken, Isidor Dab, Paul de Vuyst, Marc de Jonghe, Georges Casimir, Guy Joos, Frans de Baets, Yves Bogaerts, Jean-Luc Halloy, Pierre Bartsch, Georges Casimir, Jacques Thiriaux.

Czech Republic (226)—Petr Pohunek, Ondřej Rybníček, Olga Škopková, Ludmila Pavelková, Pavel Broź, Eva Ohnutková, Bronislava Novotná, Jiří Baĺy, Irena Krćmová, Zuzana Kuralová, Tomáš Koćí, Helena Honomichlová, Viktor Kašák, Petr Panzner, Vladimír Vondra, Jaroslava Némećková, Ester Seberová, Tomáš Śykora, Vít Petrů, Jarmila Turzíková.

Denmark (97)—Torben Sörensen, Steen Neldam, Jörgen Peter Jensenius Kludt, Ulrik Bo Hansen, Thorkild Knudsen, Paul Jörgen Schultz, Dan Rost, Flemming Jensen.

Finland (218)—Vuokko Kinnula, Pekka Saarelainen, Mirja Eho-Remes, Erkka Valovirta, Kari KK Venho, Eeva Kokko, Markku Järvinen, Tuula Toljamo, Antti Taivainen, Tuomo Kava, Jaakko Herrala, Anna-Leena Kuusela, Pertti Nordgren, Pirkko Syvänen.

France (121)—Philippe Godard, Patrick Rufin, Michel Anton, Jean-Pierre Aubert, Martine Grosclaude, Christian Brambilla, Patrick Archaud, Jean-Lousi Racineux, Jean-Francois Muir, Marc Albertini, Pascal Le Roux, Alain Simmons.

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Poland (311)—Andrzej Szczeklik, Sabina Chyrek-Borowska, Grzegorz Mincewicz, Teresa Malaczynska, Tadeusz Latos, Krystyna Obtulowicz, Andrzej Emeryk, Pawel Gorski, Dariusz Nowak, Miroslaw Szmidt, Jerzy Alkiewicz, Grzegorz Ziolo, Leonard Spychalski, Danuta Chmielewska-Szewczyk, Krystyna Nowacka, Michal Pirozynski, Halina Prokurat, Andrzej Boznanski, Jozef Malolepszy, Edmund Rogala, Jerzy Kozielski.

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United Kingdom (39)—David Weston, M. E. Johnson, Colin Barrett.

Southern Europe

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Canada (114)—John H. S. Li, Daniel Landry, Dennis O'Keefe, Bhanu F. Muram, Howard S. Conter, Douglas Tweel, Sharon D. Peters.

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Other countries

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Australia (85)—Jason Garrood, Majorie J. E. Patel, Chris Hogan, Grant Russel.

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Indonesia (196)—Hadiarto Mangunnegoro, Caecilia Arimah Wijono, Nancy Hutabarat Tobing, Nastiti N. Rahajoe, Sugito, Eddy Surjanto, Barmawi Hisyam, Hood Alsagaff, Gunadi Santosa.

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