THE STUDY IN SUMMARY

The aim of this study was to compare bambuterol oral solution administered once daily in the evening with terbutaline oral solution administered three times daily, in 2-5 year old children with asthma. The primary objective was to evaluate safety (adverse events, blood pressure, pulse rate, haematology and clinical chemistry). Plasma concentrations of terbutaline/bambuterol and activity of plasma cholinesterase were also measured. Evaluation of efficacy was a secondary objective (diary data, morning and evening: asthma symptoms, other symptoms, use of inhaled bronchodilators, the number and length of awakenings due to asthma (during the night), restlessness and PEF). The study was a multicentre study performed at 22 centres in Sweden, Denmark, Norway, Finland and France. It was double-blind, randomized and of a parallel group design. The study started with a two-week run-in period and continued with a three-month treatment period. A two-week follow-up period ended the study. There were two treatment groups; 2/3 of the patients received bambuterol oral solution 10 mg once daily in the evening and 1/3 received terbutaline oral solution 0.075 mg/kg body weight three times daily. A 50% increase or decrease in dose, depending on clinical effect and adverse events as judged by the physician, was allowed after two weeks' treatment. Only 13 patients, however, changed the dose (3 decreased and 10 increased by 50%). Further, the patients were to be 2-5 years old, boys and girls with asthma, with an intake of a single dose of an inhaled or oral bronchodilator as rescue medication ≥ 4 times a week during the run-in period when no other regular use of bronchodilators was allowed.

A total of 155 patients were randomized and treated with the study drugs i.e. 51 patients in the terbutaline group and 104 patients in the bambuterol group. Their mean age was 3.8 years.

There were no statistically or clinically significant differences between the groups concerning pulse rate, systolic and diastolic blood pressure. The changes during the study were very moderate.

There were no remarkable findings on the laboratory tests (B-Haemoglobin, B-Leucocytes,
S-ASAT, S-ALAT, S-Bilirubin, S-Creatinine, S-Potassium and B-Glucose). S-ALAT showed a slight, but statistically significant increase for both treatments.

Mean steady state plasma terbutaline concentration was 8.9 nmol/L in the terbutaline group and 10.4 nmol/L in the bambuterol group. The mean plasma bambuterol concentration in the bambuterol group was 2.1 nmol/L.

The mean plasma cholinesterase activity (nmol/min/5μL) before treatment with the study medication (visit 2) were 7.7 in the terbutaline group and 9.1 in the bambuterol group. The activity in the terbutaline group increased almost 100 % between visits 2 and 6 (end of treatment), and the activity in the bambuterol group went up by 50 %. This was probably due to the fact that the samples taken at visit 2 were frozen, while the samples taken at visit 6 were analysed within 5 hours after sampling. After a final dose at visit 6, the terbutaline group and the group with no active bambuterol (lunch medication) showed no change after 2 hours, while the group with active bambuterol (evening medication) showed a 50 % decrease, which was expected.

For PEF_{morning}, the mean increase from run-in to treatment was 16.9 L/min in the terbutaline group and 23.3 L/min in the bambuterol group. This difference, 6.4 L/min, was not significant (p=0.17). For PEF_{evening}, the mean increase was 20.2 L/min in the terbutaline group and 20.6 L/min in the bambuterol group.

Ten variables from the diary cards were analysed: Asthma Symptoms, day and night, Restlessness, day and night, Other Symptoms, day and night, Number of Inhalations, day and night, Number of Awakenings due to asthma and Total Time Awake (minutes). There were no statistically significant differences between treatment groups in any of these variables, either if analysing treatment means or percentage of symptom free days.

Further, both terbutaline and bambuterol were well tolerated and the reported adverse events were mostly mild to moderate.
Conclusion: Both bambuterol 10 mg oral solution once daily and terbutaline 0.075 mg/kg b.w. oral solution three times daily showed a good safety profile with respect to clinical and laboratory tests. Both treatments were generally well tolerated and the reported adverse events were mostly mild to moderate.

With regard to efficacy, both treatments showed a similar bronchodilating effect (PEF morning and PEF evening). The increase in morning PEF from run-in to treatment, however, was slightly larger in the bambuterol group. Thus both treatments were similar in effect and safety profile, but bambuterol, by virtue of its once daily administration, is to be preferred.