DOSE-RANGING EFFICACY AND SAFETY STUDY OF ALBUTEROL MULTIDOSE DRY POWDER INHALER (MDPI) AND ALBUTEROL HYDROFLUOROALKANE (HFA) VERSUS PLACEBO MDPI IN CHILDREN WITH ASTHMA

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Background: To evaluate the efficacy and safety of albuterol delivered via a novel, inhalation-driven, multidose dry powder inhaler (MDPI) that does not require patient coordination of device actuation with inhalation and albuterol hydrofluoroalkane (HFA) at 2 dose levels relative to placebo in children with persistent asthma. **Methods:** A phase 2, multicenter, double-blind, double-dummy, single-dose, 5-period, crossover study (ABS-AS-202; NCT01899144) randomized pediatric patients (aged 4–11 years) with persistent asthma and prestudy forced expiratory volume in 1 second (FEV_1) of 60%–90% of predicted normal to 1 of 10 treatment sequences containing albuterol MDPI (90 and 180 mcg), albuterol HFA (90 and 180 mcg), and placebo MDPI+placebo HFA. Spirometry was the primary measurement to evaluate study end points. Serial FEV_1 measurements were obtained at designated time points over 6 hours after the completion of study drug administration at each treatment visit. Safety was evaluated by adverse events. **Results:** The full analysis set included 61 patients. Baseline-adjusted percent-predicted FEV_1-time curve over 6 hours postdose ($PPFEV_1$ AUC_{0-6}) was significantly greater in all active treatment groups compared with placebo ($P \leq 0.0107$; **Table**). $PPFEV_1$ AUC_{0-6} was similar in the albuterol MDPI 90 mcg and 180 mcg groups (**Table**); however, the albuterol HFA 180 mcg group had significantly greater $PPFEV_1$ AUC_{0-6} than the albuterol HFA 90 mcg group ($P=0.0226$; **Table**). All doses of albuterol were generally well tolerated. **Conclusions:** Albuterol MDPI significantly improved pulmonary function versus placebo in children with asthma. Improvements for albuterol MDPI 90 and 180 mcg were similar; a dose-response effect was observed with albuterol HFA. Results suggest that relief of asthma symptoms in children may be managed adequately with albuterol MDPI (1–2 inhalations). No new safety concerns were noted with albuterol MDPI, and its safety profile is consistent with that of albuterol HFA.

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Table. Baseline-adjusted $PPFEV_1$ AUC_{0-6} (%•hour; full analysis set)

	Placebo N=61	**Albuterol MDPI 90 mcg N=61**	**Albuterol MDPI 180 mcg N=61**	**Albuterol HFA 90 mcg N=61**	**Albuterol HFA 180 mcg N=61**
n	59	58	59	59	59
Mean ± SE	25.4 ± 6.25	46.6 ± 6.27	48.0 ± 6.24	37.9 ± 6.25	49.1 ± 6.26
95% CI	12.94, 37.81	34.13, 59.07	35.56, 60.39	25.43, 50.30	36.61, 61.50
Active-Placebo					
Mean ± SE		21.2 ± 4.87	22.6 ± 4.87	12.5 ± 4.85	23.7 ± 4.85
95% CI		11.62, 30.81	13.00, 32.20	2.93, 22.05	14.13, 33.23
P-value		<0.0001	<0.0001	0.0107	<0.0001
90 mcg-180 mcg					
Mean ± SE			-1.4 ± 4.88		-11.2 ± 4.87
95% CI			-11.00, 8.23		-20.80, -1.59
P-value			0.7772		0.0226

AUC_{0-6}, area under the curve over 6 hours; CI, confidence interval; HFA, hydrofluoroalkane; MDPI, multidose dry powder inhaler; $PPFEV_1$, percent predicted forced expiratory volume in 1 second; SE, standard error.