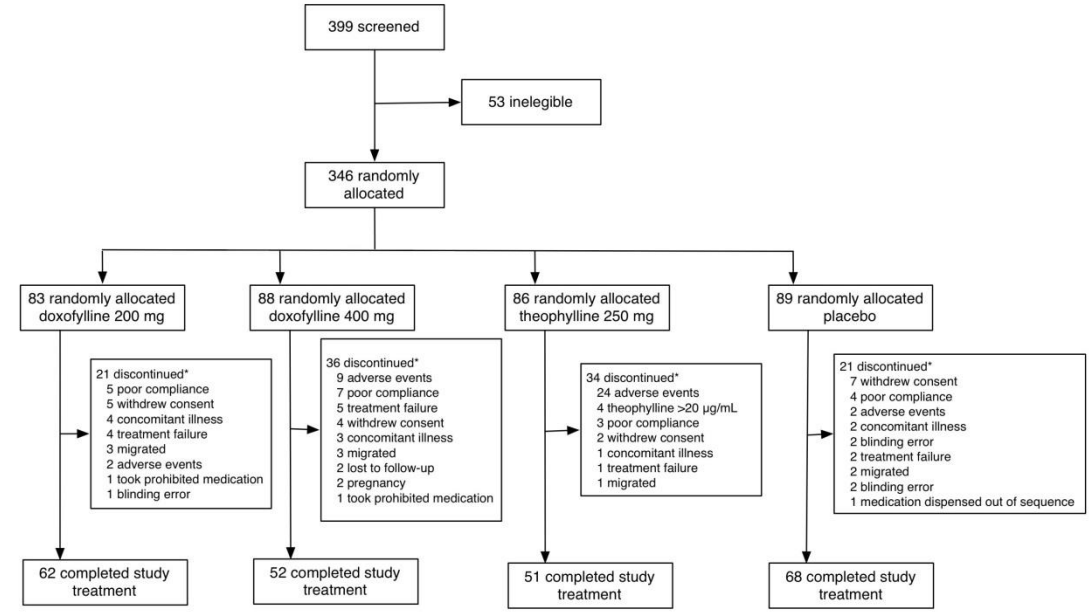
Participant flow



* The investigator could specify more than one reason for withdrawal; subjects with more than one reason for withdrawal are counted under each reason that applied.

Datasets analyzed:

	Doxofylline 200 mg	Doxofylline 400 mg	Theophylline 250 mg	Placebo
Intent-to-Treat Subjects[a]	83	88	86	89
Evaluable Subjects[b]	80	82	82	82
Reasons Nonevaluable:				
Study medication unblinded	3	2	2	3
Protocol violation	0	4	2	4

[a]Intent-to-treat subjects were those who were randomized and treated in the double-blind period.
[b]Evaluable subjects were those who fulfilled the requirements of the protocol.

Baseline Characteristics

Summary of demographic and baseline data (Intent-to-Treat Subjects):

	Doxofylline 200 mg	Doxofylline 400 mg	Theophylline 250 mg	Placebo
Number of subjects	83	88	86	89
Age (yr)				
Mean (SEM)	33.0 (1.5)	36.6 (1.4)	36.0 (1.5)	36.4 (1.3)
Sex				
Male	44 (53.0%)	44 (50%)	38 (42.2%)	44 (49.4%)
Female	39 (47.0%)	44 (50%)	48 (55.8%)	45 (50.6%)
Race				
Caucasian	69 (83.1%)	70 (79.5%)	74 (86.0%)	76 (85.4%)
Black	3 (3.6%)	7 (8.0%)	4 (4.7%)	5 (5.6%)
Hispanic	10 (12.0%)	7 (8.0%)	8 (9.3%)	7 (7.9%)
Other	1 (1.2%)	4 (4.5%)	0 (0%)	1 (1.1%)
Body Weight (kg)				
Mean (SEM)	79.13 (1.90)	78.85 (1.97)	78.84 (1.92)	82.95 (1.79)
Height (cm)				
Mean (SEM)	171.06 (1.29)	169.70 (1.10)	168.04 (1.53)	171.80 (1.03)
% of Predicted FEV_1				
Mean (SEM)	66.2 (1.2)	64.5 (1.1)	66.4 (1.1)	64.9 (1.1)
No. of Asthma Attacks/Wk				
Mean (SEM)	7.98 (0.99)	8.51 (1.12)	9.69 (1.50)	7.62 (1.13)
Precipitating Factors				
Yes	82 (98.8%)	86 (97.7%)	83 (96.5%)	86 (96.6%)
No	1 (1.2%)	2 (2.3%)	3 (3.5%)	3 (3.4%)
Hospitalizations for Asthma				
Yes	32 (38.6%)	37 (42.0%)	36 (41.9%)	33 (37.1%)
No	51 (61.4%)	51 (58.0%)	49 (57.0%)	56 (62.9%)
Age at Onset of Asthma (yr)				
Mean (SEM)	13.90 (1.50)	16.10 (1.40)	16.80 (1.70)	18.00 (1.60)
Years Since Onset				
Mean (SEM)	19.00 (1.40)	20.20 (1.40)	19.20 (1.40)	18.40 (1.50)

SEM = standard error of mean

Outcome Measures

Primary outcome:

Percent Increases in FEV_1 at primary endpoint[a] (change from baseline in the value recorded 2 h after dose administration).

Treatment	n	Mean (SEM)
Doxofylline 200 mg	83	12.6 (2.8)
Doxofylline 400 mg	88	12.4 (2.5)*
Theophylline 250 mg	84	15.6 (2.1)**
Placebo	89	7.5 (2.4)

*<0.05, **P<0.01 vs. placebo (two-way analysis of variance).
[a] Combined results from each subject's last visit during the active-treatment period, regardless of when it occurred.

Secondary outcomes

Percent Increases in FEV_1 at week 12 (change from baseline in the value recorded 2 h after dose administration).

Treatment	n	Mean (SEM)
Doxofylline 200 mg	61	13.0 (3.1)
Doxofylline 400 mg	52	14.9 (3.5)*
Theophylline 250 mg	51	17.4 (2.9)*
Placebo	68	6.1 (2.1)

*<0.05 vs. placebo (two-way analysis of variance).

Change from baseline in asthmatic attack (n of attacks/day)

	Week 12		Primary endpoint[a]	
Treatment	n	Mean (SEM)	n	Mean (SEM)
Doxofylline 200 mg	61	-0.47±0.14	81	-0.42±0.14
Doxofylline 400 mg	52	-0.68±0.18*	80	-0.56±0.13*
Theophylline 250 mg	51	-0.57±0.20*	79	-0.87±0.18*
Placebo	68	-0.16±0.13	88	-0.14±0.13

*<0.05, **P<0.01 vs. placebo (two-way analysis of variance).
[a] Combined results from each subject's last visit during the active-treatment period, regardless of when it occurred.

Change from baseline in albuterol use rate (puffs/day)

	Week 12		Primary endpoint[a]	
Treatment	n	Mean (SEM)	n	Mean (SEM)
Doxofylline 200 mg	61	-0.85±0.28	81	-0.87±0.26*
Doxofylline 400 mg	52	-1.33±0.35*	80	-1.05±0.25*
Theophylline 250 mg	51	- 1.10±0.39*	79	- -1.72±0.36*
Placebo	68	- 0.16±0.27	88	-0.16±0.27

*<0.05, **P<0.01 vs. placebo (two-way analysis of variance).
[a] Combined results from each subject's last visit during the active-treatment period, regardless of when it occurred.

Adverse Events

Serious adverse events (participants affected/at risk)

	Doxofylline 200 mg	Doxofylline 400 mg	Theophylline 250 mg	Placebo
Total serious adverse events	1/83	1/88	1/86	1/89
Severe asthma	0/83	0/88	1/86	0/89
Noncardiologic episode of unknown etiology	1/83	0/88	0/86	0/89
Degenerative disc disease	0/83	0/88	0/86	1/89
Asthma attack	0/83	1/88	0/86	0/89

Deaths: no subjects died during the study or within 30 days after finishing the study.

Adverse events (participants affected/at risk)

	Doxofylline 200 mg	Doxofylline 400 mg	Theophylline 250 mg	Placebo
Subjects with one or more adverse event	41/83	46/88	54/86	39/89
Body as a whole disorders				
Headache	23/83	25/88	25/86	24/89
Overdose	0/83	0/88	4/86	0/89
Abdominal pain	1/83	4/88	3/86	3/89
Chest pain	0/83	5/88	0/86	1/89
Cardiovascular disorders				
Palpitations	1/83	4/88	4/86	0/89
Digestive disorders				
Diarrhoea	3/83	3/88	5/86	4/89
Dyspepsia	3/83	6/88	9/86	4/89
Nausea	9/83	12/88	25/86	13/89
Vomiting	5/83	3/88	6/86	2/89
Nervous system disorders				
Dizziness	5/83	4/88	6/86	4/89
Insomnia	2/83	5/88	14/86	1/89
Nervousness	1/83	7/88	14/86	3/89
Somnolence	2/83	1/88	1/86	5/89
Respiratory system disorders				
Asthma	5/83	2/88	2/86	1/89
Pharyngitis	4/83	2/88	0/86	2/89
Rhinitis	4/83	3/88	2/86	5/89