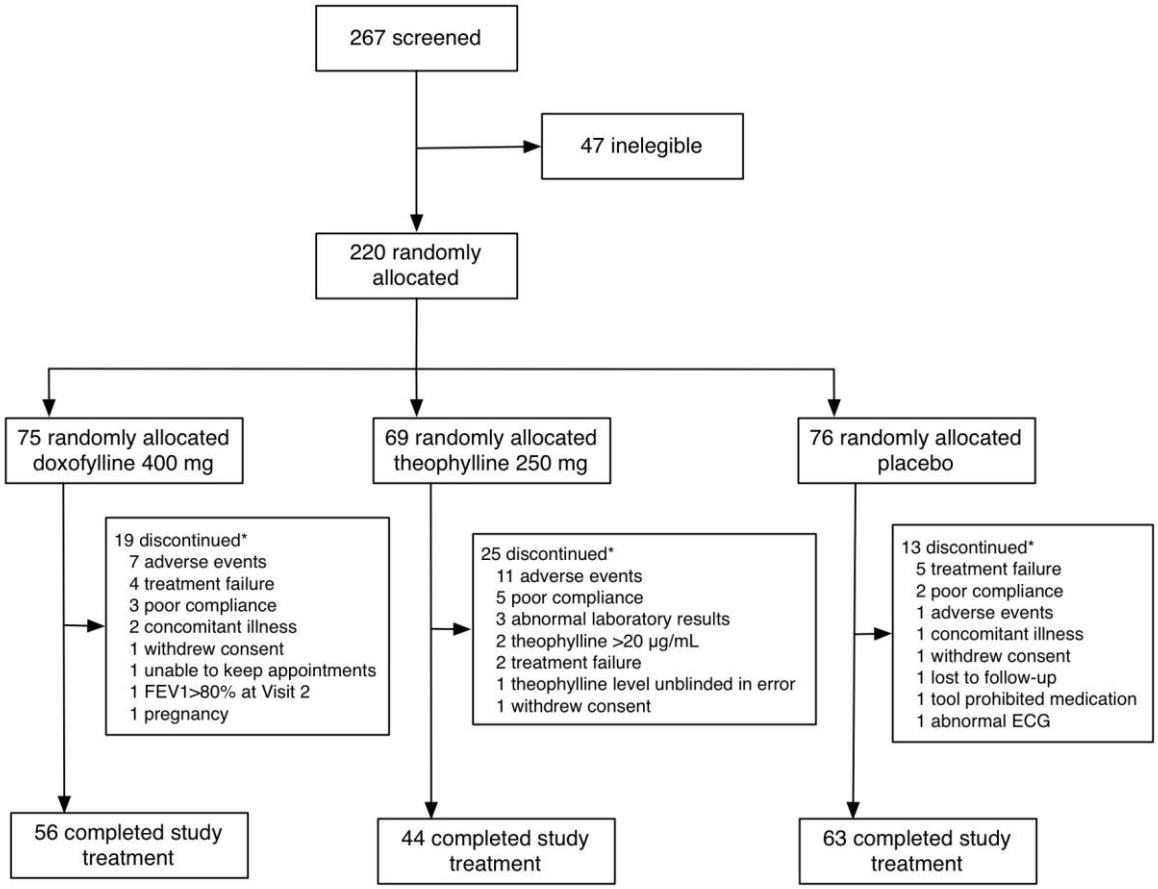
Participant flow



* 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.

1. Datasets analyzed:

	Doxofylline 400 mg	Theophylline 250 mg	Placebo
Intent-to-Treat Subjects[a]	75	69	76
Evaluable Subjects[b]	75	68	74
Reasons Nonevaluable:			
Protocol violation	0	1	2

[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 400 mg	Theophylline 250 mg	Placebo
Number of subjects	75	69	76
Age (yr)			
Mean (SEM)	35.8 (1.3)	36.7 (1.5)	37.6 (1.6)
Sex			
Male	35 (46.7%)	32 (46.4%)	31 (40.8%)
Female	40 (53.3%)	37 (53.6%)	45 (59.2%)
Race			
Caucasian	69 (92.0%)	57 (82.6%)	69 (90.8%)
Black	3 (4.0%)	8 (11.6%)	4 (5.3%)
Hispanic	3 (4.0%)	4 (5.8%)	2 (2.6%)
Other			
Body Weight (kg)			
Mean (SEM)	80.30 (2.31)	81.33 (2.19)	77.74 (2.04)
Height (cm)			
Mean (SEM)	167.21 (1.73)	167.43 (1.89)	166.15 (2.05)
% of Predicted FEV_1			
Mean (SEM)	66.3 (1.2)	66.8 (1.2)	67.2 (1.0)
No. of Asthma Attacks/Wk			
Mean (SEM)	6.75 (0.94)	7.37 (0.93)	5.99 (0.88)
Precipitating Factors			
Yes	74 (98.7%)	67 (97.1%)	71 (93.4)
No	1 (1.3%)	2 (2.9%)	5 (6.6%)
Hospitalizations for Asthma			
Yes	34 (45.43%)	28 (40.6%)	31 (40.8%)
No	41 (54.7%)	41 (59.4%)	45 (59.2%)
Age at Onset of Asthma (yr)			
Mean (SEM)	13.7 (1.6)	14.30 (1.6)	17.90 (2.0)
Years Since Onset			
Mean (SEM)	22.20 (1.5)	22.4 (1.6)	19.7 (1.5)

SEM = standard error of mean

Outcome measures

Primary outcome measure:

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 400 mg	75	13.6 (2.6)
Theophylline 250 mg	66	16.0 (2.9)
Placebo	76	9.6 (2.4)

[a] Combined results from each subject's last visit during the active-treatment period, regardless of when it occurred.

Secondary outcome measures:

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 400 mg	52	17.8 (3.1)
Theophylline 250 mg	42	13.7 (3.8)
Placebo	61	10.4 (2.8)

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

	Week 12		Primary endpoint[a]	
Treatment	n	Mean (SEM)	n	Mean (SEM)
Doxofylline 400 mg	59	-0.43±0.18	72	-0.33±0.16
Theophylline 250 mg	43	-0.57±0.12	63	-0.65±0.12*
Placebo	64	-0.46±0.15	74	-0.28±0.16

*<0.05 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 400 mg	59	-0.9±0.34	72	-0.65±0.32
Theophylline 250 mg	43	-1.19±0.25	63	-1.32±0.24
Placebo	64	-1.01±0.32	74	-0.59±0.36

[a] Combined results from each subject's last visit during the active-treatment period, regardless of when it occurred.

2. Safety evaluation:

Serious adverse events (participants affected/at risk)

	Doxofylline 400 mg	Theophylline 250 mg	Placebo
Total serious adverse events	2/75	0/69	0/76
Systemic reaction to immunotherapy	1/75	0/69	0/76
Cold leading to asthma exacerbation	1/75	0/69	0/76

Deaths: no subjects died during the study or shortly after finishing the study.

Adverse events

(Participants affected/at risk)

	Doxofylline 400 mg	Theophylline 250 mg	Placebo
Subjects with one or more adverse event	48/75	44/69	43/76
Body as a whole disorders			
Asthenia	0/75	4/69	4/76
Headache	21/75	22/69	20/76
Overdose	0/75	4/69	0/76
Abdominal pain	2/75	1/69	5/76
Digestive disorders			
Diarrhoea	4/75	2/69	8/76
Dyspepsia	6/75	5/69	3/76
Nausea	13/75	18/69	7/76
Vomiting	5/75	3/69	1/76
Nervous system disorders			
Dizziness	4/75	1/69	3/76
Insomnia	8/75	5/69	2/76
Nervousness	1/75	9/69	4/76
Respiratory system disorders			
Asthma	5/75	5/69	7/76
Cough increased	1/75	4/69	3/76
Pharyngitis	1/75	5/69	4/76
Rhinitis	5/75	4/69	4/76