ISRCTN10030693 https://doi.org/10.1186/ISRCTN10030693

Assessing the long-term efficacy and safety of doxofylline in treating asthma

Submission date
28/03/2019

Recruitment status
No longer recruiting

Registration date
01/04/2019

Overall study status
Completed

Last Edited
05/04/2019

Condition category
Respiratory

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Doxofylline is a drug belonging to the class methylxanthines. Doxofylline has shown similar efficacy to theophylline in asthmatic patients but with significantly fewer side effects. Recent findings from two clinical trials (DOROTHEO1 and DOROTHEO2) performed in asthmatic patients and lasting 12 weeks showed that doxofylline has a favorable efficacy and safety profile, and that this drug provides a meaningful improvement of lung function. Unlike other xanthines such as theophylline, doxofylline does not activate certain specific cellular receptors (i. e. adenosine receptors) and does not alter the movement of calcium into cells. These specific characteristics may account for the favorable safety profile of doxofylline. The the main anti-asthmatic effects of doxophylline seems to be related with its activity on intracellular enzymes (i. e. phosphodiesterases). Thus, the aim of this study is to investigate the efficacy and safety profile of doxofylline administered for long time, up to one year, in asthmatic patients.

Who can participate?
Adult (over 18 years old) asthmatic patients

What does the study involve?
All participants received for 12 months oral doxofylline 400 mg three times daily . Lung function tests were carried out at day 1 and at months 1, 3, 6, 9, and 12.

What are the possible benefits and risks of participating?
The possible benefits may include increased lung function, reduced asthma events rate, and reduced use of albuterol, leading to an overall increased asthma control. The potential risks may include the occurrence of side effects, namely gastrointestinal symptoms (nausea, vomiting, gastrointestinal distress, stomach ache), tachycardia or palpitations, insomnia, and nervousness. In any case, the overall treatment benefits would overcome the symptoms related with the side effects.

Where is the study run from?
Allergy Associates, Inc., North Dartmouth, MA (US); Allergy, Asthma & Immunology Center of Rochester, Rochester, NY (US); International Medical Technical Consultants, Inc., Prairie Village, KS (US); Advanced Allergy & Asthma, Albany, NY (US); Pulmonary Associates, Philadelphia, PA

(US); Allergic Disease Associates, Philadelphia, PA (US); Doctors' Clinic Research Center, Vero Beach, FL (US); Pharmaco Health Research Center, Austin, TX (US); Cleveland Clinic, Cleveland, OH (US); Piedmont Research Associates, Inc., Winston-Salem, NC (US); Chicago Center for Clinical Research, Chicago, IL (US); National Association for Clinical Research, Philadelphia, PA (US); Washington University School of Medicine Research Office, St. Louise, MO (US).

When is the study starting and how long is it expected to run for?
February 1992 to September 1994

Who is funding the study?
Roberts Pharmaceutical Corporation (USA)

Who is the main contact?
Dr Alberto Giraudi
alberto.giraudi@abcfarmaceutici.it

Contact information

Type(s)
Scientific

Contact name
Dr Alberto Giraudi

ORCID ID
https://orcid.org/0000-0003-0456-069X

Contact details
Via Canton Moretti, 29
Località San Bernardo Ivrea (TO)
Italy
10090
+39 (0)125 240111
alberto.giraudi@abcfarmaceutici.it

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
30,722-303C

Study information

Scientific Title

A Long-term clinical trial on the Efficacy and Safety profile of Doxofylline in Asthma: the LESDA study

Acronym
LESDA

Study objectives
Doxofylline may have a favorable efficacy and safety profile when administered for a longer time.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/11/1991, Northeast Medical Research Associates Institutional Review Board (49 State Road, Watuppa Building North Dartmouth, MA, USA 02747; 1-855-636-7287; study@nemra-us.com), ref: 30,722-303C-91.

Study design
Multicenter, open-label, single-arm , phase III, clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Asthma

Interventions
This is a single-arm study in which asthmatic patients received doxofylline 400 mg (Maxivent 400 mg, tablets; Lot # Dox-049-11/E) three times daily (t.i.d, drug administered at 8 hr interval) administered per os. The total duration of treatment was 12 months, and the follow up lasted 13 months

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Doxofylline

Primary outcome(s)
Airway obstruction is measured using “FEV1, detected via pulmonary” function tests at day 1 and months 1, 3, 6, 9, 12.

Key secondary outcome(s))

1. The change from baseline (T0, hour 0) in FEV1 values is measured “via pulmonary function tests” at months 1, 3, 6, 9 and 12.
2. Asthma events rate (total number of events divided by the total number of days on study medication), and albuterol use rate (total number of puffs divided by total number of days on study medication) are determined using Medication/Symptom Diaries at “months 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12.”
3. Safety is assessed by physical examinations, ECGs, and the recording of vital signs, laboratory test results, and adverse events “(AE) at months 1, 3, 6, 9 and 12.”
3.1. All “clinical AE” entered on the Case Report Forms (CRFs) are classified as to possible relation to study medication (not related, possibly related, definitely related, or unknown) and severity (mild, moderate, or severe).
3.2. Also recorded for each AE are the start and stop dates, the action taken (none, study medication discontinued, or treatment prescribed), and the outcome (recovered, recovered with sequelae, under treatment, deceased, unknown, or ongoing).
3.3. If a subject experiences an AE leading to withdrawal from the study, the investigator is to make an effort to have the subject return to the study centre for examination and obtain a serum sample for drug level determination. The time and date of the last dose taken is to be entered into the CRF.

Completion date
04/06/1997

Eligibility

Key inclusion criteria
1. Males and non-pregnant females.
1.1. Women of childbearing potential had to use acceptable methods of birth control and have a negative prestudy serum β-hCG pregnancy test.
1.1.1. Acceptable methods of birth control were limited to vaginal or intrauterine contraceptive devices or agents and natural (postmenopausal) or surgical sterility.
2. 18 years of age or older.
3. Nonsmokers for at least 6 months before entering the study.
4. In good physical condition with a more than 1-year history of chronic, extrinsic reversible hyperreactive airway disease (asthma).
5. On screening, had a baseline FEV1 value within 50% to 80% of the predicted FEV1 value for their age and height, when immediate-release theophylline or sustained-release theophylline had been withheld for at least 24 hours.
6. On screening, at least a 15% increase in FEV1 30 minutes after administration of a standard dose (2 puffs, 180 µg) of albuterol.
7. Stable dose of inhaled corticosteroids (ICS) and/or cromolyn sodium for at least 30 days was permitted. If ICS and/or cromolyn sodium was required during the study, it was recommended that a Doxofylline baseline level be achieved (minimum, 14 days) before the administration of any additional medications.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Clinically significant deviation from normal in physical examination, laboratory parameters, ECG, or chest x-ray, as evaluated by the Principal Investigator, that would have precluded the subject's participation in the study
2. Clinically significant coexisting disease, including:
2.1. Cardiovascular disease, including a history of congestive heart failure, angina pectoris, or myocardial infarction within 1 year
2.2. Convulsive disorder
2.3. Gastrointestinal disease
2.4. Renal disease
2.5. Hepatic disease
2.6. Hematologic disease
2.7. Insulin-dependent diabetes mellitus
2.8. Nonreversible chronic pulmonary disease
2.9. Known infection with human immunodeficiency virus
2.10. Chronic obstructive pulmonary disease
3. Presence of any acute illness
4. Sensitivity to theophylline or theophylline-like agents
5. A resting heart rate of less than 50 bpm or greater than 100 bpm and/or an arterial blood pressure of less than 100/60 mmHg or greater than 140/90 mmHg when sitting
6. History of alcohol, narcotic, barbiturate, marijuana, or polydrug abuse
7. Participation in other investigational drug studies within 30 days before the start of this study, except the DOROTHEO1 (ISRCTN65297911) and DOROTHEO2 (ISRCTN22374987) that preceded this study.
8. Subjects using oral steroids or oral B2-agonists
9. Lactating females

Date of first enrolment
19/02/1992

Date of final enrolment
07/09/1994

Locations

Countries of recruitment
United States of America

Study participating centre
Allergy Associates, Inc.
North Dartmouth

United States of America
02747

Study participating centre
Allergy, Asthma & Immunology Center of Rochester, P.C
Rochester
United States of America
14620

Study participating centre
International Medical Technical Consultants, Inc.
Prairie Village
United States of America
64108

Study participating centre
Advanced Allergy & Asthma
Albany
United States of America
12203

Study participating centre
Pulmonary Associates
Philadelphia
United States of America
United States of America

Study participating centre
Allergic Disease Associates
Philadelphia
United States of America
19107

Study participating centre
Doctors' Clinic Research Center
Vero Beach
United States of America
32960

Study participating centre
Pharmaco Health Research Center
Austin
United States of America
78705

Study participating centre
Cleveland Clinic
Cleveland
United States of America
44113

Study participating centre
Piedmont Research Associates, Inc.
Winston-Salem
United States of America
27103

Study participating centre
Chicago Center for Clinical Research
Chicago
United States of America
60634

Study participating centre
National Association for Clinical Research
Philadelphia
United States of America
19114

Study participating centre
Washington University School of Medicine Research Office
St. Louis
United States of America
43617

Sponsor information

Organisation
Roberts Pharmaceutical Corporation

Organisation
ABC farmaceutici

Organisation
Takeda (United States)

ROR
https://ror.org/03bygaq51

Funder(s)

Funder type
Industry

Funder Name
Roberts Pharmaceutical Corporation

Funder Name
ABC farmaceutici

Results and Publications

Individual participant data (IPD) sharing plan
Dr Alberto Giraudi (alberto.giraudi@abcfarmaceutici.it) can be contacted for accessing to the datasets. Available data include patient-by-patient variable recorded at each time-point and will be available for request in one year from the publication of the paper. Informed consent was obtained by all the participants of the study. Data will be shared merely for scientific purposes (i. e. post-hoc analyses, pooled analyses) with researchers employed at institutional research departments who will make a formal request to the scientific board of ABC Farmaceutici. If the scientific board determine the proposed analysis is consistent with the local ethics and legal rules, and could provide further evidence than those published, the data will be released in agreement with patients' anonymisation. The data will be available for one year from the date of publication in a high-impact peer reviewed journal.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		30/03/2019	01/04/2019	No	No