Efficacy and safety of aclidinium bromide/formoterol fumarate fixed-dose combinations compared with individual components and placebo when administered to patients with stable chronic obstructive pulmonary disease (COPD).

Published: 11-08-2011
Last updated: 28-04-2024

• To assess the long-term bronchodilation of aclidinium/formoterol FDCs compared to individual components and placebo, when administered twice daily via inhalation to COPD patients.• To assess the benefits of aclidinium/formoterol FDCs in COPD…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON38263

Source
ToetsingOnline

Brief title
Almirall ACLIFORM-COPD

Condition

- Bronchial disorders (excl neoplasms)

Synonym
COPD, progressive respiratory disease

Research involving
Human

Sponsors and support

Primary sponsor: Almirall
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: Aclidinium bromide/Formoterol fumarate, COPD, Holter, Spirometry

Outcome measures

Primary outcome

• Co-primary efficacy variables (at Week 24 on treatment):

- Change from baseline in morning pre-dose (through) FEV1 of each

aclidinium/formoterol

FDC dose compared to formoterol monotherapy 12 µg.

- Change from baseline in 1-hour post-morning dose FEV1 of each

aclidinium/formoterol FDC

dose compared to aclidinium monotherapy 400 µg.

Secondary outcome

• Secondary efficacy variables (at Week 24 on treatment):

- Improvement of TDI focal score of each aclidinium/formoterol FDC dose

compared to

placebo.

- Change from baseline in SGRQ total score of each aclidinium/formoterol FDC

dose

compared to placebo.

Study description

Background summary

This aclidinium/formoterol Fix dose combination (FDC) is expected to provide superior bronchodilation compared with either component, aclidinium and formoterol, alone and with placebo. Furthermore, administration of 2 bronchodilators in a FDC via a single inhaler may improve treatment compliance compared with that associated with the use of 2 separate inhalers.

Study objective

• To assess the long-term bronchodilation of aclidinium/formoterol FDCs compared to individual components and placebo, when administered twice daily via inhalation to COPD patients.

• To assess the benefits of aclidinium/formoterol FDCs in COPD symptoms, disease-related health status and COPD exacerbations compared to individual components and placebo, when administered twice daily via inhalation to COPD patients.

• To evaluate the long-term safety and tolerability of aclidinium/formoterol FDCs compared to individual components and placebo when administered twice daily via inhalation to COPD patients.

Study design

Patients will visit the clinic to sign the informed consent form and will perform the Screening Visit.
However, certain COPD medications are prohibited for this trial purposes thus, in case the patient is
treated with any of those, after signing the informed consent form and before conducting any
assessment at the Screening Visit, the patient will remain in wash-out for a period that will vary from 1
day to 1 month depending on the specific medication to be washed out.

At Screening Visit inclusion and exclusion criteria will be checked by means of patient*s medical
history review, COPD status, physical examination, laboratory, blood pressure and ECG
measurement.

Two to three weeks later, patients still fulfilling inclusion/exclusion criteria will perform the

Randomisation Visit (Visit 1). At this visit, a 24 week-long treatment period will start. During this
treatment period each patient will inhale one dose, twice daily, from one out of the five possible
treatments (in a double-blind fashion).

Patients found to be eligible for inclusion in the study, will be randomly allocated (like randomly flipping a coin) to one of five treatments arms:
-aclidinium/formoterol FDC 400/12 µg;
aclidinium/formoterol FDC 400/6 µg;
-aclidinium monotherapy 400 µg;
-formoterol monotherapy 12 µg or
-placebo (dummy treatment containing no active ingredient).

The distribution of this random allocation of patients to the study treatment arms is 2:2:2:2:1, respectively. That means that ther is a 1 out of 9 chance to receive placebo.

After Randomisation Visit, patients will attend 5 more visits. The first visit will take place 1 week after
the start of the study treatment period, then at 4, 12, 18 and 24 weeks on treatment (from Visit 2 to
Visit 6).

At the different visits over the treatment period, pre-morning dose assessments will include:
Pulmonary Function Test (PFT), blood pressure and ECG measurement, Baseline/Transition
Dyspnoea Index (BDI/TDI), St. George*s Respiratory Questionnaire (SGRQ) and EuroQol
questionnaire-5D (EQ-5D). Post-morning dose assessments will be performed over the next 3 hours
and will include PFTs, blood pressure and ECG measurement.

Laboratory test will be repeated at 12 weeks on treatment (Visit 4) and at the end of the treatment
period (Visit 6). Also at Visit 6, a physical examination will be repeated.
Two weeks after the last study drug administration (even in case of premature discontinuation), every
patient will attend a last visit to the clinic (Visit 7) or either receive a follow-up phone call from the site
(as deemed appropriate by the investigator) in order to assess any on-going or new adverse events.
Patients will be provided with relief medication (salbutamol pMDI 100µg/puff) to be used on an as
needed basis, from the time of the informed consent signature until the end of treatment period (Visit

6).

From Screening Visit to the end of the treatment period (Visit 6), patients will use, twice daily, an electronic Patient Diary to record the intake of study drug and relief medication as well as COPD symptoms by means of the EXACT questionnaire (evening) or the Night-time and Early morning COPD symptoms questionnaire (morning). Patients will also use a paper Patient Diary to record any adverse event and the intake of any concomitant medications from Screening Visit until Follow-up Contact (Visit 7).

During the entire duration of the study adverse events (including COPD exacerbations) and the use of any concomitant medication will be assessed and recorded by the investigator. In addition to the assessments described above, a subset of 20% of the total patients will have 24-hour ECG Holter recording at Screening Visit and at 12 and 24 weeks on study treatment. Thus, these patients will need to attend the clinic on 2 consecutive days in 3 occasions to either place or remove the Holter device.

In a different subset of 20% of total patients, additional spirometry assessments will be performed at Randomisation Visit and at 12 and 24 weeks on treatment. On these days, spirometries will continue up to 12 hours post-morning dose.

Intervention

Inhalation of powder.

Study burden and risks

It is possible that the disease during this trial get worse or even does not improve. The chance your symptoms worsening is more while receiving the placebo treatment. The treatment with aclidinium bromide/formoterol can also have consequences for the future health of the patient, which are not predictable at this moment.

No specific risk is anticipated with the doses and the dose regimen proposed for this study.

Contacts

Public
Almirall

Laurea Miro 408-410
Sant Feliu de LLobregat, Barcelona 08980
ES
Scientific
Almirall

Laurea Miro 408-410
Sant Feliu de LLobregat, Barcelona 08980
ES

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Adult male and female patients aged >=40.
• Patients with stable moderate to severe COPD (GOLD guidelines): Screening Postbronchodilator
test FEV1/FVC < 70% and FEV1 >=30 and < 80% of predicted normal value.
• Current or ex*smokers of >=10 pack-years.
• Patients who were never randomised in a study involving aclidinium/formoterol fixed-dosecombination (Almirall project code 40464).
• Patients previously randomised in aclidinium monotherapy trial (Almirall project code 34273) are
allowed in this study only if time elapsed since the finalisation of the previous trial treatment is at

least 6 months prior to the Screening Visit.

Exclusion criteria

• Patients with history or current diagnosis of asthma
•Patients with no signs of a COPD exacerbation within 6 weeks prior to the screening visit
• Patients with evidence of clinically significant respiratory and/or cardiovascular conditions or
laboratory abnormalities.
• Patients who are expected to start a pulmonary rehabilitation program during the trial, or those who finished or started it within 3 months prior to the Screening Visit.
• Patients with contraindication to anticholinergic drugs such as bladder neck obstruction, acute
urinary retention, symptomatic non-stable prostatic hypertrophy or (known) narrow-angle glaucoma.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-01-2012
Enrollment:	44
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aclidinium bromide 400 μg
Generic name:	Aclidinium bromide
Product type:	Medicine
Brand name:	Aclidinium bromide/Formoterol Fumarate 400/12 μg fixed-dose combination
Generic name:	Aclidinium bromide/Formoterol Fumarate
Product type:	Medicine
Brand name:	Aclidinium bromide/Formoterol Fumarate 400/6 μg fixed-dose combination
Generic name:	Aclidinium bromide/Formoterol Fumarate
Product type:	Medicine
Brand name:	Formoterol Fumarate 12 μg
Generic name:	Formoterol Fumarate

Ethics review

Approved WMO Date:	11-08-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-11-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-12-2011
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-02-2012
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-04-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-10-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-10-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-12-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2011-0001524-3-NL
CCMO	NL37481.060.11