

To evaluate the effect of inhaled medication together with exercise and activity training on exercise capacity and daily activities in patients with chronic lung disease with obstruction of airways (PHYSACTO™)

This is a summary of a clinical study in Chronic Obstructive Pulmonary Disease (COPD). It is written for the general public. It includes information about how researchers did the study and what the results were.

We thank all patients who took part in this study. Through your participation, you helped researchers answer important questions about tiotropium and olodaterol and the treatment of COPD.



What was this study about?

This study compared 4 treatments for COPD. One treatment involved inhaling 2 medicines (tiotropium and olodaterol), starting to exercise, and making lifestyle changes. A second treatment involved inhaling 2 medicines (tiotropium and olodaterol) and making lifestyle changes. The third treatment involved inhaling 1 medicine only (tiotropium) and making lifestyle changes. The fourth treatment involved making lifestyle changes only.

Researchers measured the physical fitness (in terms of exercise capacity) of patients who took treatments including medicines. They also measured the physical fitness of patients who took the treatment including lifestyle changes only. At the end of the study, the treatments including medicines were compared with the treatment including lifestyle changes only.

This study started in March 2014 and ended in October 2015.



Why was the study needed?

COPD is a disease that makes it difficult to breathe. It causes wheezing, shortness of breath, and chest tightness. Patients often have a cough that produces mucus. COPD is usually caused by smoking cigarettes.

Many people with COPD find it hard to stay physically active. Physical activity makes them feel out of breath. However, it is important for patients with COPD to stay active and exercise. Otherwise, their symptoms might get worse. Researchers wanted to find out what treatments help patients increase physical fitness.



Which medicines were studied?

Researchers studied 2 medicines that widen the airways.

Tiotropium is used to treat COPD. Olodaterol is also used to treat COPD. Both medicines help to open the airways and keep them open all day long (long-acting bronchodilators). This makes it easier for patients to breathe.

Both medicines are used separately or combined together (a fixed-dose combination) for the treatment of COPD. These medicines come as a solution that needs to be inhaled using a special inhaler called the Respimat®. This inhaler converts the solution into a soft mist. Patients breathe in this soft mist to take the medicines.

Placebo inhalers looked like the other inhalers tested but did not contain any medicine.



Who participated in the study?

Patients with COPD took part in the study. All had to be current or ex-smokers between the ages of 40 and 75 years.

Overall 303 patients were treated; 200 were men and 103 were women. On average patients were 65 years old. The youngest patient was 41 years old. The oldest patient was 75 years old.

The table below shows the number of patients by geographical region and country.

Geographical region	Countries	Number of patients
Western Europe	Austria, Belgium, Denmark, Germany, Portugal, United Kingdom	189
North America	Canada, United States	62
Australia/New Zealand	Australia, New Zealand	35
Eastern Europe	Poland	17



How was this study done?

Patients were divided into 4 groups. Each patient had an equal chance of being in a certain group. The patients in each group received a different treatment or combination of treatments as follows:

Combination 1: Patients took 2 puffs of combined tiotropium and olodaterol every day (5 µg tiotropium/5 µg olodaterol per day). They used the Respimat® inhaler to take their medicine. Patients were encouraged to make lifestyle changes. They also took exercise classes.

Combination 2: Patients took 2 puffs of combined tiotropium and olodaterol every day (5 µg tiotropium/5 µg olodaterol per day). They used the Respimat® inhaler to take their medicine. Patients were also encouraged to make lifestyle changes.

Tiotropium: Patients took 2 puffs of tiotropium every day (5 µg tiotropium per day). They used the Respimat® inhaler to take their medicine. Patients were also encouraged to make lifestyle changes.

Placebo: Patients took 2 puffs of placebo every day. They used the Respimat® inhaler to take placebo. Patients were also encouraged to make lifestyle changes.

The chart below provides a summary of the different treatments and their components.

	Combination 1	Combination 2	Tiotropium	Placebo
Tiotropium + Olodaterol (12 weeks)	✓	✓		
Tiotropium only (12 weeks)			✓	
Lifestyle changes (12 weeks)	✓	✓	✓	✓
Exercise (3 times per week for 8 weeks)	✓			

Patients in the group that received exercise training knew what treatment they received. This is because they were the only group that received exercise training. The patients in the other groups did not know which medicine they received. The doctors did not know either.

Patients visited their doctors regularly during the 12 weeks of the study. During the visits, the doctors collected information on each patient's health.

Patients also took tests to find out how fit they were at doctor visits. One test was called the endurance shuttle walk test at 85% of predicted maximum oxygen consumption. During this test, each patient walked a constant, brisk speed. This speed was directly related to the individual patient's maximum speed. Even though some patients walked faster and others walked slower, all patients walked at the same relative speed. Researchers measured the time each patient could walk during this test before needing to stop due to symptoms. Researchers were particularly interested in the results of this test after 8 weeks of treatment.

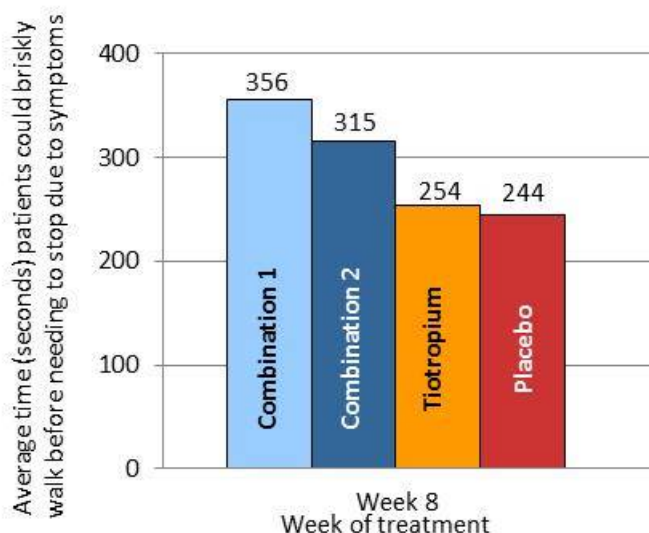


What were the results of this study?

Patients who took combinations 1 or 2 were more physically fit than those who took placebo. They could walk for a longer time before needing to stop due to symptoms than patients who took placebo. Patients who took tiotropium were not more physically fit than those who took placebo. Patients in the tiotropium and placebo groups walked a similar time before needing to stop due to symptoms.

More specifically, patients who took combination 1 walked 46% longer than patients who took placebo. Patients who took combination 2 walked 29% longer than patients who took placebo. Researchers did statistical tests on these results. It is unlikely that the difference between the combination 1 and placebo groups came about by chance. It is also unlikely that the difference between the combination 2 and placebo groups came about by chance. Statistical tests showed that it was more likely than not that the difference between the tiotropium and placebo groups came about by chance.

These results (Week 8) are illustrated in the graph below.





Were there any unwanted effects?

Unwanted effects are any health problems that the doctors thought were caused by the study medicines. A total of 2 out of 76 patients (2.6%) in the combination 1 group had unwanted effects. In the combination 2 group, 3 out of 76 patients (3.9%) had unwanted effects. In the tiotropium group 6 out of 76 patients (7.9%) had unwanted effects. Finally, 4 out of 75 patients (5.3%) in the placebo group had unwanted effects. The most common unwanted effects are shown in the table below.

	Combination 1 (76 patients)	Combination 2 (76 patients)	Tiotropium (76 patients)	Placebo (75 patients)
Patients with any unwanted effect	2 patients (2.6%)	3 patients (3.9%)	6 patients (7.9%)	4 patients (5.3%)
Dry throat	1 patient (1.3%)	1 patient (1.3%)	3 patients (3.9%)	0 patients
Flare-up of COPD (COPD)	0 patients	1 patient (1.3%)	1 patient (1.3%)	3 patients (4.0%)

Some unwanted effects were serious because they required a visit to hospital or a longer stay in hospital. Others were serious if they led to disability or death. Unwanted effects were also serious if the doctor thought they were serious for any other reason. In this study, 1 patient in the placebo group had a serious unwanted effect. No patients in the combination 1, combination 2, or tiotropium groups had serious unwanted effects.



Are there follow-up studies?

No follow-up studies are currently planned.

If more clinical studies with tiotropium and olodaterol are done, they may be found on the public websites listed below. To search for these studies, use the following names:

Tiotropium + olodaterol FDC Respimat®

 **Where can I find more information?**

You can find the scientific summaries of the study results at these websites:

www.trials.boehringer-ingelheim.com search for the study number: BI 1237.16

www.clinicaltrialsregister.eu/ctr-search search for the EudraCT number: 2013-002671-18

www.clinicaltrials.gov search for the NCT number: NCT02085161

The sponsor of this study was Boehringer Ingelheim.

The full title of the study is:

An exploratory, 12 week, randomised, partially double-blinded, placebo-controlled, parallel group trial to explore the effects of once daily treatments of orally inhaled tiotropium + olodaterol fixed dose combination or tiotropium (both delivered by the Respimat® inhaler), supervised exercise training and behaviour modification on exercise capacity and physical activity in patients with Chronic Obstructive Pulmonary Disease (COPD) [PHYSACTO™]

This was a Phase III study.

Important notice

This summary shows only the results from one study and may not represent all of the knowledge about the medicine studied. Usually, more than one study is carried out in order to find out how well a medicine works and the side effects of the medicine. Other studies may have different results.

You should not change your therapy based on the results of this study without first talking to your treating physician. Always consult your treating physician about your specific therapy.

Boehringer Ingelheim has provided this lay summary in accordance with European Union transparency obligations.

© Boehringer Ingelheim International GmbH.