

## *Dear Reader,*

This is a summary of a clinical study in patients with schizophrenia. It is written for the general reader and uses language that is easy to understand. It includes information about how researchers did the study and what the results were. The simplified title for the study is: 'A study to test how effective and well tolerated a 12-week treatment of BI 409306 is in patients with schizophrenia'. The results of this study may not apply to everybody. The study started in December 2014 and ended in June 2016. The sponsor of this study was Boehringer Ingelheim.

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We thank all patients who took part in this study. Through your participation, you helped researchers answer important questions about BI 409306.

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## What was the study about?

The researchers wanted to know how well 4 different doses of a new medicine called BI 409306 would improve the ability to think clearly and accurately in patients with schizophrenia. The study also looked at how well patients tolerated BI 409306.

## Why was the research needed?

Schizophrenia is a brain disorder. Patients with schizophrenia may:

- Have strange thoughts and behaviours.
- Have problems thinking clearly and accurately.
- See or hear things that are not real.

Medicines are available that may lessen some of the symptoms of schizophrenia. However, there is a strong need for medicines that directly treat the causes of schizophrenia or the problems with thinking clearly and accurately. Unclear thinking may affect attention, memory, learning, and managing daily tasks.

This study looked at the effects of BI 409306 on patients' ability to think clearly and accurately after they took BI 409306 in addition to their usual schizophrenia medicine for 12 weeks.

## Which medicines were studied?

The new medicine tested in the study is called BI 409306. It blocks the action of a protein called phosphodiesterase 9A (PDE9A). Blocking the action of PDE9A improves signalling in certain parts of the brain that are important for memory and learning. BI 409306 is being tested in patients with schizophrenia for its effects on the ability to think clearly and accurately.

In the study, researchers tested the effects of 4 different doses of BI 409306 tablets versus placebo tablets in patients with schizophrenia. The placebo tablets looked exactly like BI 409306 tablets, but had no active medicine in them.

## What did the researchers want to know?

Researchers wanted to know if taking BI 409306 helped patients with schizophrenia improve their ability to think clearly and accurately. Patients took a set of special tests called the MCCB several times during the study. The MCCB stands for Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery. These tests measure processing speed, attention, learning, memory, problem solving, and social awareness. The result of the tests was a number value called the MCCB score. Changes in the MCCB score over time can show changes in the ability of patients with schizophrenia to think clearly and accurately. The researchers looked at the results of the tests after 12 weeks of taking study medicine (BI 409306 or placebo).

Researchers also collected information on the side effects of BI 409306 and placebo during the study.

## Who participated in the study?

The study treated a total of 516 patients with schizophrenia. All patients had stable symptoms (in the residual phase of their illness) for at least 8 weeks before the study began. Patients were already taking certain other medicines to treat schizophrenia symptoms. The average age was 42.3 years. The youngest patient was 19 years old and the oldest patient was 56 years old. Most of the patients (69.8%) were men. Patients were from North America (411 patients from Canada and the United States), Asia (82 patients from Japan, Malaysia, and Taiwan), and Europe (23 patients from Germany).

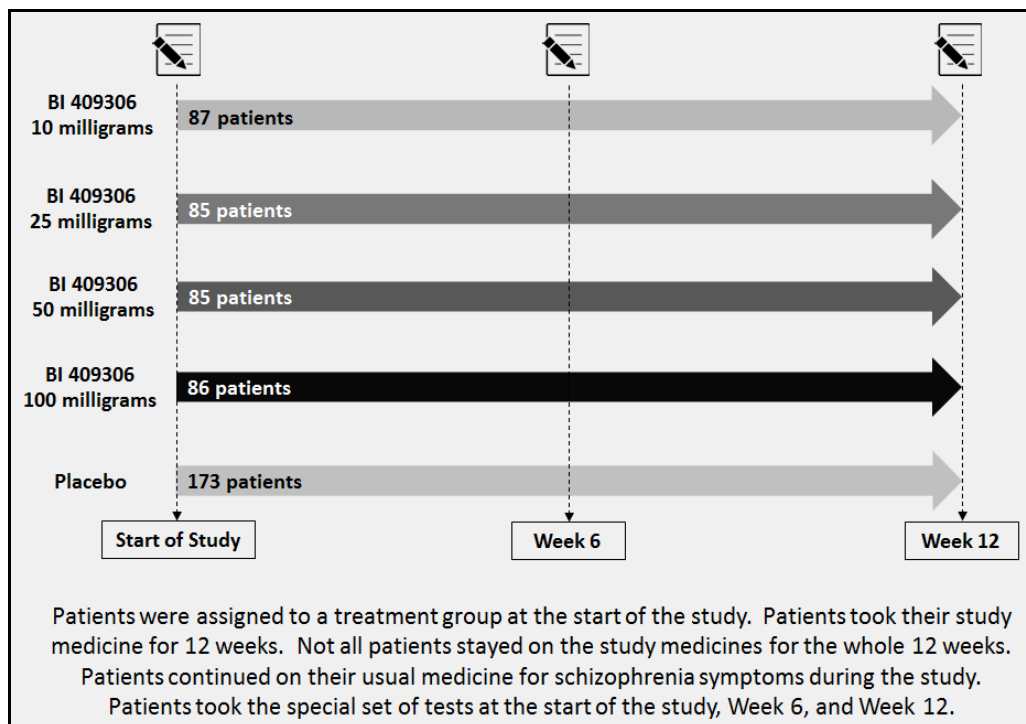
## How was this study performed?

Patients were divided into 5 groups. It was decided by chance who got into each group (randomised). The patients and the study doctors did not know who took which medicine. This is called a 'double-blind design'. The patients in 4 of the groups took different doses of BI 409306. The patients in the fifth group took placebo.

All patients followed the same general procedures:

- Patients took BI 409306 or placebo by mouth once daily for 12 weeks.
- Patients continued on their usual medicine for schizophrenia symptoms during the study.
- Patients visited the study doctor about every 3 weeks.
- Patients took a special set of tests called the MCCB a few times during the study.
- Study doctors collected information about side effects.

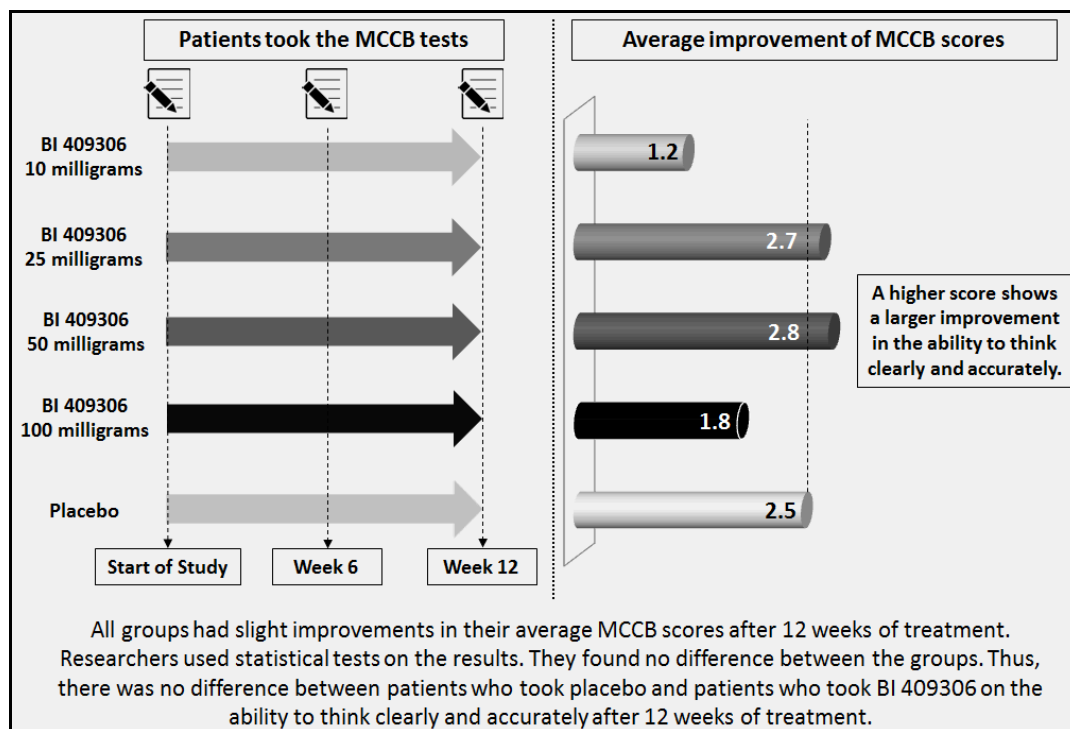
The dose and the number of patients treated in each group are shown in the picture below.



## What were the results of this study?

Did BI 409306 work well at improving how well patients with schizophrenia could think compared to placebo (change in MCCB score)?

No. After 12 weeks of treatment, patients who took BI 409306 did not show larger improvements in their ability to think clearly and accurately compared to patients who took placebo. Researchers used statistical tests on the results to check if the results were reliable. They found no difference between the treatment groups. The picture on the next page shows the average improvement in MCCB score.



## Which side effects did patients have?

A side effect is any medical problem seen during a study. Some side effects are caused by the study medicines, some are caused by other medicines taken by the patient, some are caused by the disease, and some have yet a different cause. Some side effects may be seen in a lot of patients, while other side effects may be seen in only a few patients. Some side effects may be temporary and go away after time, while other side effects may last a very long time or even be permanent. Researchers keep track of all medical problems patients have during a study.

Ninety-eight patients (19.0%) had side effects that the study doctors thought were related to the study medicine. The number of patients with side effects that study doctors thought were related to BI 409306 was higher in patients who took higher doses of BI 409306. The percentage of patients with side effects that study doctors thought were related to study medicines was similar in the placebo group and the BI 409306 10 mg group. Most of the side effects that the study doctors thought were related to study medicines were mild or moderate. The table on the next page shows related side effects that happened in 4 or more patients in any group.

	BI 409306				Placebo (173 patients)
	10 mg (87 patients)	25 mg (85 patients)	50 mg (85 patients)	100 mg (86 patients)	
Patients with related side effects	11 patients (12.6%)	15 patients (17.6%)	16 patients (18.8%)	34 patients (39.5%)	22 patients (12.7%)
Visual brightness	0	2 patients (2.4%)	3 patients (3.5%)	6 patients (7.0%)	0
Sensitive to light (Photophobia)	0	2 patients (2.4%)	2 patients (2.4%)	6 patients (7.0%)	2 patients (1.2)
Headache	3 patients (3.4%)	3 patients (3.5%)	2 patients (2.4%)	0	4 patients (2.3%)
Blurred vision	1 patient (1.1%)	3 patients (3.5%)	1 patient (1.2%)	4 patients (4.7%)	2 patients (1.2%)
Dizziness	0	1 patient (1.2%)	2 patients (2.4%)	4 patients (4.7%)	0
Colour vision not normal (Chromatopsia)	0	0	0	4 patients (4.7%)	0

Serious side effects are side effects that made the patient go to the hospital or stay in the hospital. Or these side effects needed urgent attention by a doctor, were life-threatening, or led to the death of the patient. Ten patients (5.8%) in the placebo group had serious side effects. None of the patients in the BI 409306-treated groups had serious side effects. Therefore, none of the serious side effects seen in the study were caused by BI 409306 treatment.

## Are there follow-up studies?

No follow-up studies are planned.

## Where can I find more information?

The protocol number of the study is 1289.6. The full title of the study is:

‘A Phase II randomised, double-blinded, placebo-controlled study to evaluate the efficacy, safety, and tolerability of four orally administered doses of BI 409306 during a 12-week treatment period in patients with schizophrenia on stable antipsychotic treatment’.

Please visit the following website to find a scientific summary of the study results:

[http://trials.boehringer-ingelheim.com/trial\\_results.html](http://trials.boehringer-ingelheim.com/trial_results.html).

You can find more details at [www.clinicaltrialsregister.eu](http://www.clinicaltrialsregister.eu) by searching for the EudraCT number 2013-005015-28 or at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) by searching for the NCT number NCT02281773.

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## 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.

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