Summary of Clinical Study Results

A study to learn about the effectiveness and safety of seltorexant compared with quetiapine, when taken with routine antidepressant treatment in adults with depression with insomnia symptoms

Thank you!

The sponsor would like to thank those who participated in this clinical study of seltorexant.

You helped our researchers learn more about the possible effectiveness and safety of seltorexant compared with quetiapine, when taken with routine antidepressant treatment in participants with depression with insomnia symptoms.

This summary is written for the participants in this study using non-technical language that is clear and easy to understand. It is important to know that this summary only describes the results from a single study and other studies may have different results. Researchers and health authorities need to consider the results of many studies to understand if an investigational medicine is safe and effective for the use in which it is being studied.

The products in this study may not be approved where you live or for the use being studied. Doctors should refer to the full prescribing information, where applicable, for proper use of these products.

It is essential that you do not make any health care decision based on the results of this study. Always talk to a doctor before making any health care decisions, or if you have any questions about these study results. Nothing in this summary should be viewed as prescribing information or medical advice, and no conclusions about any products or health care options should be made based on this summary.

In this summary, 'sponsor' refers to the company that takes responsibility for the study. 'Researchers' refers to the sponsor, and the doctors and staff at study sites.

Contents of this summary

What was the purpose of this study?

Depression with insomnia symptoms

Depression, sometimes known as major depressive disorder, is a common mood disorder. It causes a lasting feeling of sadness and a loss of interest in everyday activities. The way a person with depression feels, thinks, and acts can interfere with work, social life, and family life.

Approximately one of three people with depression does not improve enough with routine antidepressant treatments. For those people, there is an increased chance of experiencing difficulty sleeping (insomnia). In turn, the insomnia symptoms can lead to more depression.

Other treatments are needed for people with depression with insomnia symptoms that have not improved with routine antidepressant medicines. Researchers are working to find treatments that could be added to existing medicines. Potential add-on treatments first need to be tested for effectiveness and safety.

Treatments studied

Seltorexant is an investigational medicine that is being tested for its effects on depression with insomnia symptoms. Investigational medicines are studied to see whether they could be used as medicines.

Quetiapine is a commonly used medicine that is given to some people for whom depression has not improved with antidepressant therapy alone.

In this study, the participants took seltorexant or quetiapine as capsules by mouth. They also continued their routine antidepressant treatment.

Aim of the study

In this study, researchers wanted to learn about the effectiveness and safety of seltorexant compared with quetiapine when either was added to existing antidepressant treatment in participants experiencing depression with insomnia symptoms. Participants in this study were those for whom their current antidepressant treatment was only partially effective in easing their symptoms.

Within a single study, researchers usually want to answer several questions. In this study, the main question was:

After 26 weeks of treatment, what percentage of participants who took seltorexant responded to treatment compared with the participants who took quetiapine?

The severity of the symptoms of depression was measured using a scale called the Montgomery-Asberg Depression Rating Scale (MADRS). Participants were considered to have 'responded' to treatment if they had at least a 50% decrease in their MADRS score.

In addition, researchers were searching for information that would help in understanding the safety of seltorexant in people with depression with insomnia symptoms.

Where and when was this study done?

This study included 756 participants in 15 countries/territories. The table below shows the number of participants in each region.

Number of participants by region

Region	Countries/Territories	Number of participants
Americas	Argentina, Canada, United States	312
Asia	Malaysia	22
Europe	Belgium, Bulgaria, Czech Republic, Latvia, Lithuania, Poland, Russia, Serbia, Slovakia, Ukraine, United Kingdom	422

This study started in September 2020 and ended in October 2023, so the entire study lasted about 3 years. An individual study participant could be in the study for up to about 8 months.

The researchers completed this study as planned. When the study ended, the sponsor reviewed the data and created a report of the results. This is a summary of the main results in that report.

Who was in this study?

The researchers invited people with depression with insomnia symptoms to participate in the clinical study.

All participants:

- only had some improvements of depression symptoms on their current routine antidepressant treatment.
- had not received more than two prior antidepressant treatments in their current episode of depression.
- had moderate to severe insomnia symptoms

In total, 74% (558 out of 756) of participants were females and 26% (198 out of 756) of participants were males.

All participants were between 18 and 74 years of age.

What happened during this study?

This was a Phase 3 study. In Phase 3 studies, an investigational medicine is tested for its effects and safety in a large number of patients with the condition being studied.

The study compared seltorexant with quetiapine.

Researchers used a computer program to put participants in two different treatment groups in a random way. This means that each person had an equal chance of ending up in either treatment group.

This study was “double-blind”. This means that neither the participants nor the researchers knew who received which treatment. This was done to make sure that the study results were not influenced by this knowledge.

The study was divided into three parts.

Screening (up to 1 month): The researchers checked if the participants met the requirements to take part in this study based on their medical history and health.

Treatment (up to 26 weeks): Participants took seltorexant or quetiapine capsules by mouth daily each night in addition to their routine antidepressant treatment.

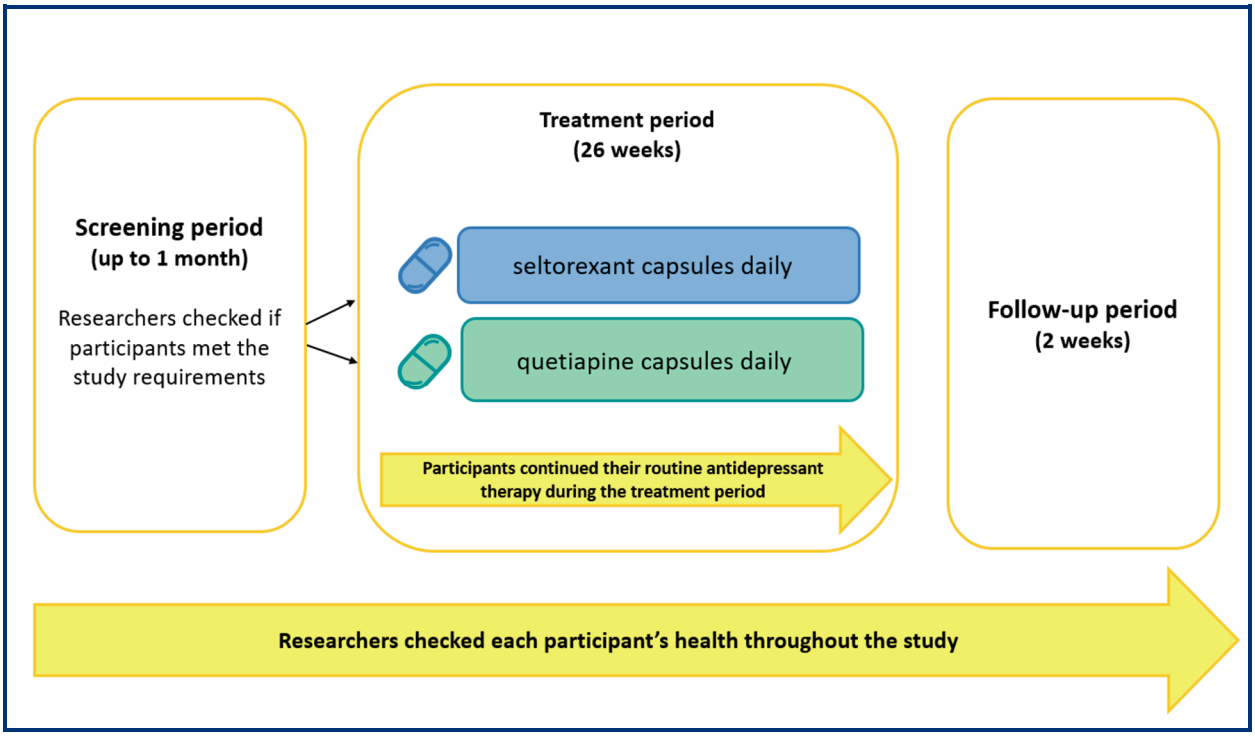
Participants in the quetiapine treatment group initially started on a low dose and then had their dose increased, following the local treatment guidelines for quetiapine use. Afterwards, the study doctors assessed effectiveness and safety of the participants’ treatment and increased or decreased the quetiapine dose accordingly.

Participants were also given placebo capsules to keep the study double-blinded. A placebo looks like the medicines and is taken in the same way but does not have any medicine in it. This ensured that the two groups of study participants took the same number of capsules.

Follow-up (up to 2 weeks): The researchers checked each participant's health after they received their last dose of study treatment.

The following figure shows the overview for the treatment period.

Treatment overview



During the study, the researchers regularly measured participants' severity of symptoms of depression and insomnia by asking the participants certain questions. The researchers also asked participants to fill out questionnaires that measured their own perceptions of their symptoms. More information on these assessments can be found on the websites listed at the end of this summary.

What were the main results of this study?

This is a summary of the main results from this study. It does not show separate results for individual participants. An individual's results could be different from those of the total group of participants.

After 26 weeks of treatment, what percentage of participants who took seltorexant responded to treatment compared with the participants who took quetiapine?

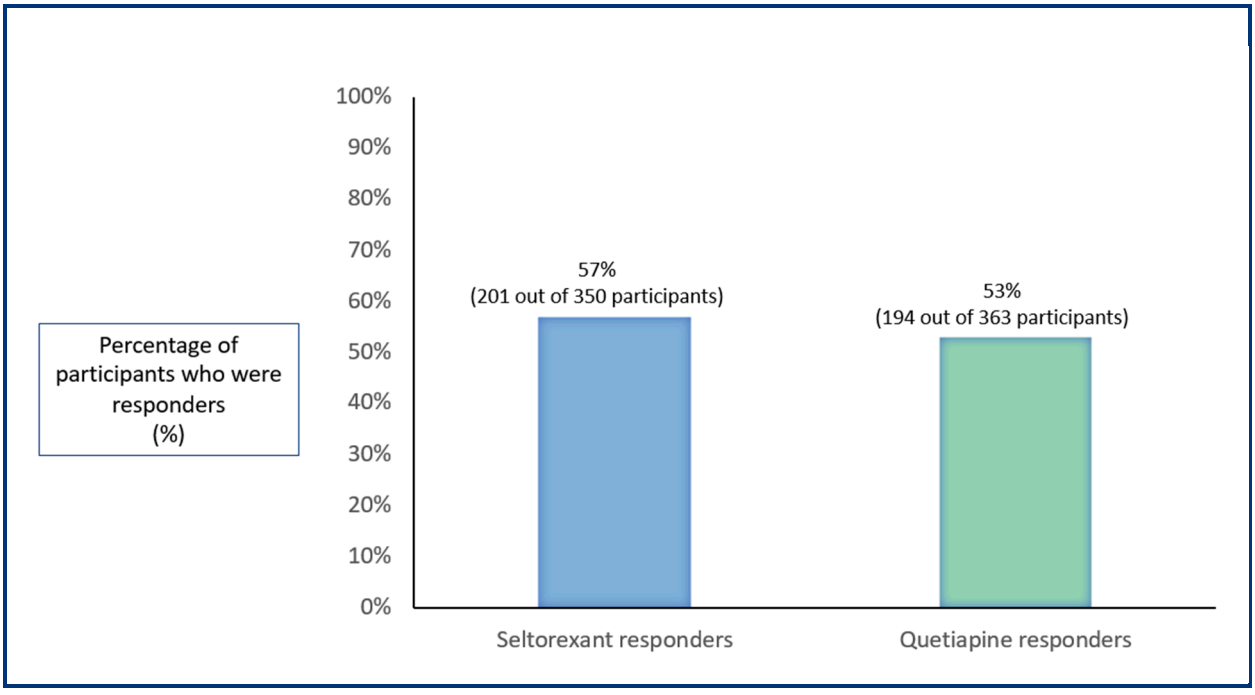
To answer this question, the researchers recorded the participants' MADRS scores throughout the study. The MADRS is a 10-item questionnaire that doctors use to measure the severity of depression symptoms and to identify changes brought on by antidepressant treatment. Each item is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total possible score of 60. Higher scores represent more severe symptoms, and lower scores indicate less severe symptoms.

Researchers compared the participants' MADRS scores before taking treatment and after 26 weeks of treatment. Then, they compared the percentage of participants in both groups who responded to study treatment.

Participants were considered to have 'responded' to study treatment if they had at least a 50% decrease in their MADRS score.

The figure below shows the percentage of participants who responded after 26 weeks of treatment.

Percentage of participants who responded after 26 weeks of treatment



After 26 weeks of treatment, a similar percentage of participants in both treatment groups responded to study treatment. The difference between treatment groups was too small for the researchers to know if there was any difference in the effect of treatments.

These results do not include 43 participants:

- Results from participants with a low MADRS score before taking treatment were excluded.
- Results from some participants in Ukraine could not be included due to the Russia-Ukraine conflict.

Researchers also completed an analysis of the main question including results from participants who had a low MADRS score before taking treatment. The results of this analysis were similar to the results in the previous figure.

This summary only describes the results of the main study question. Information on further questions the researchers asked can be found at the websites listed at the end of this summary.

What possible side effects were observed during this study?

Adverse events are medical problems that can happen to participants during a study. Study doctors record all these adverse events whether they are related to investigational medicines or not. The websites listed at the end of this summary will have more information about the adverse events that happened in this study.

This summary only considers the results of this single study. Researchers need to consider the results of many studies to understand if any adverse events may be related to the investigational medicine.

For the purpose of this summary, **possible side effects** are adverse events that happened during the study, that the **study doctor thought might be related to study treatment**.

At the time the study doctor made their assessment they did not know whether the participant was receiving seltorexant or quetiapine.

This section is a summary of the possible side effects for this study. Different possible side effects may be described in other documents, after the sponsor collects the results of more than one study.

No serious possible side effects (for example, those that are disabling, require inpatient hospital care, are life-threatening, or cause death) were reported for any of the participants. No participants died during the study.

What were the most common possible side effects?

The table below shows the most common possible side effects observed in at least 2% of participants in either treatment group.

Percentage (number) of participants with the most common possible side effects observed in at least 2% of participants in either treatment group

	Seltorexant (out of 366 participants)	Quetiapine (out of 390 participants)
Had at least one possible side effect	**29% (106)**	**52% (201)**
Feeling sleepy	6% (21)	24% (92)
Weight increased	4% (16)	12% (48)
Headache	4% (14)	4% (15)
Dry mouth	3% (10)	9% (35)
Feeling very tired	3% (9)	5% (21)
Nausea	1% (5)	3% (10)
Increased appetite	1% (5)	2% (8)
Feeling sleepy or sedated	1% (2)	5% (19)
Daytime sleepiness	Less than 1% (1)	3% (11)

How many participants had to stop study treatment because of possible side effects?

Some participants stopped seltorexant or quetiapine use because of a possible side effect. The table below shows the possible side effects that led to 1% or more of participants in either treatment group stopping study treatment.

Percentage (number) of participants who stopped seltorexant or quetiapine use due to possible side effects (1% or more of participants in either treatment group)

	Seltorexant (out of 366 participants)	Quetiapine (out of 390 participants)
Had at least one possible side effect that led to stopping the use of the study treatment	**4% (15)**	**11% (42)**
Feeling sleepy	1% (3)	5% (20)
Feeling very tired	1% (2)	2% (6)
Feeling sleepy or sedated	1% (2)	2% (8)
Daytime sleepiness	Less than 1% (1)	1% (5)

How was this study useful?

This study helped researchers learn about the effectiveness and safety of seltorexant compared with quetiapine when either was added to existing antidepressant treatment in participants experiencing depression with insomnia symptoms.

At the time of finalizing this summary, additional clinical studies with seltorexant are ongoing.

Please remember that this summary only describes results from a single study. Other studies may have different findings. Researchers need to consider the results of many studies to understand the effectiveness and safety of any investigational medicine.

You should always talk to a doctor before making any health care decisions or if you have any questions about these study results.

Thank you to those who participated in this clinical study.

Where can I learn more about this study?

If you were a study participant and you have questions about the results of this study, please speak with the doctor or staff at your study site.

You can find more information about this study on the following websites:

- www.clinicaltrials.gov — Use the study identifier NCT04513912 (US NCT number)
- www.clinicaltrialsregister.eu/ctr-search/search — Use the study identifier 2020-000341-14 (EudraCT number)

Please note that information on websites may be presented in a different way from this summary.

Full study title: A double-blind, randomized, parallel-group study with quetiapine extended release as comparator to evaluate the efficacy and safety of seltorexant 20 mg as adjunctive therapy to antidepressants in adult and elderly patients with major depressive disorder with insomnia symptoms who have responded inadequately to antidepressant therapy

Investigational medicine studied: Seltorexant (JNJ-42847922)

Protocol number: 42847922MDD3005

Date of this summary: 20 August 2024

Sponsor:

Sponsor company	Countries/Territories
Janssen Farmaceutia, S.A.	Argentina
Janssen-Cilag International NV	Belgium, Bulgaria, Czech Republic, Latvia, Lithuania, Poland, Serbia, Slovakia, United Kingdom
Janssen Research & Development LLC	Canada, Malaysia, United States
Janssen Pharmaceutica NV	Ukraine, Russia

Sponsor contact information: PLS-Admin@its.jnj.com

This Plain Language Summary of Clinical Study Results is the only sponsor-authorized version.

This document is for your personal information. The sponsor does not give any right for any information in this Plain Language Summary to be used for any other purposes, such as posting or discussing on social media, in connection with any research and/or development programs, or for providing goods or services. This document does not contain enough information for submission to any health authority. You may not use this information for any regulatory purpose, including submitting any information to any regulatory authority anywhere in the world seeking an authorization of any kind for any health care products.