Summary of Clinical Trial Results

A Phase 3 24-week study of balovaptan compared with placebo in adults with autism with a 2-year open label extension

See the end of the summary for the full title of the study.

About this summary

This is a summary of the results of a clinical trial (called a 'study' in this document) – written for:

- members of the public and
- people who took part in the study.

This summary is based on information known at the time of writing.

The study started in August 2018 and stopped early in July 2020 because the medicine being studied did not work as well as expected.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies with the same medicine.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

Contents of the summary

Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about autism and the medicine studied – called 'balovaptan'.

Key information about this study

- This study was done to see whether a medicine, called 'balovaptan', could help with socialisation and communication in autistic adults.
- In this study, people were given either balovaptan or a placebo. Who received the medicine and who received the placebo was decided randomly, or by chance.
- This study included 322 people in six countries, however, only 321 people were given balovaptan or placebo due to the study being stopped early.
- The main finding was that balovaptan did not improve socialisation and communication in autistic adults.
- No participants in the balovaptan or the placebo groups had serious side effects.
- This study stopped early because the medicine being studied did not work as well as expected.

1. General information about this study

Why was this study done?

Autism is a common and lifelong condition. Autistic people often experience difficulties with socialisation and communication, which may lead to lower quality of life (as a result of possible social isolation, reduced physical health, and associated mental health conditions) compared with people without autism. At the moment, there are no medicines available to support the socialisation and communication difficulties experienced by autistic people.

In an earlier study, the medicine 'balovaptan' was shown to improve socialisation and communication in autistic adults.[1] Researchers wanted to learn more by studying balovaptan in a larger number of autistic adults over a longer period of time.

1. Bolognani F, et al. Science Translational Medicine 2019; 11: eaar7838.

- Reference available here: https://pubmed.ncbi.nlm.nih.gov/31043521/

What was the medicine being studied?

- A medicine named 'balovaptan' ('bah – low – vap – tan') was the focus of this study.
- Balovaptan may reduce the effect of a hormone called vasopressin in the brain.
- Vasopressin has multiple roles in the body and plays an important role in the brain in socialisation and communication – some studies have shown that reducing the effects of vasopressin may improve socialisation and communication.

- This may mean that taking balovaptan could lead to improvement in socialisation and communication.

Balovaptan was compared with a 'placebo' ('plah – see – bo').

- The placebo looked the same as balovaptan but did not contain real medicine. This means it had no medicine-related effect on the body.
- Researchers compared the medicine being studied to the placebo so they could show which benefits or side effects were actually caused by the medicine.

What did researchers want to find out?

- Researchers did this study to compare balovaptan with a placebo to see how well balovaptan worked (see section 4 "What were the results of the study?").
- They also wanted to find out how safe the medicine was – by checking how many people had side effects and by seeing how serious they were (see section 5 "What were the side effects?").

The main question that researchers wanted to answer was:

1. Can balovaptan improve socialisation and communication in people with autism?

What kind of study was this?

This study was a 'Phase 3' study. This means that balovaptan had been tested in a smaller number of autistic people before this study took place. In this Phase 3 study, a larger number of autistic people took either balovaptan or a placebo. After a Phase 3 study, a decision can be made by governments regarding whether balovaptan can be approved for doctors to give to autistic individuals.

The study was 'randomised'. This means which people in the study took balovaptan and which took a placebo was decided by chance – like tossing a coin. Randomly choosing which medicine people take makes it more likely that the types of people in both groups (for example, age and race) will be a similar mix across each group. Apart from the exact medicines being tested in each group, all other aspects of care were the same between the groups.

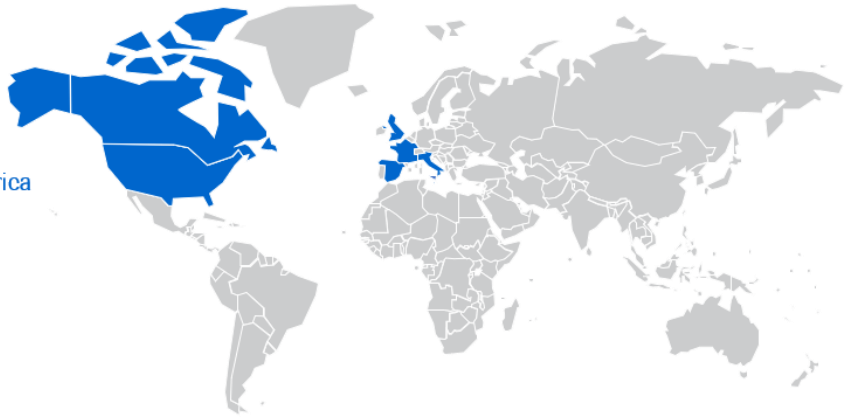
This was a 'double-blind' study. This means that neither the people taking part in the study or the study doctors knew whether participants received balovaptan or a placebo.

When and where did the study take place?

The study started in August 2018 and stopped early because balovaptan did not work as well as expected. This summary presents the results of the study up until the time it was stopped in July 2020.

The study took place at 46 study centres across six countries. The countries were: Canada, France, Italy, Spain, the United Kingdom, and the United States of America.

- Canada
- France
- Italy
- Spain
- United Kingdom
- United States of America



2. Who took part in this study?

In this study, 322 people took part. Overall, 321 people with autism received either balovaptan (163 people) or a placebo (158 people) due to the study being stopped early.

People who took part in the study were 18 years of age and over. 257 of the 321 people (80%) were male and 64 of the 321 people (20%) were female.

People could take part in the study if:

- They had a score of greater than or equal to 66 on the Social Responsiveness Scale™, second edition (SRS-2).
    - The SRS-2 scale includes 65 questions completed by a caregiver and measures the presence and severity of challenges in social behaviour.
- They were over 18 years of age.

People could not take part in the study if:

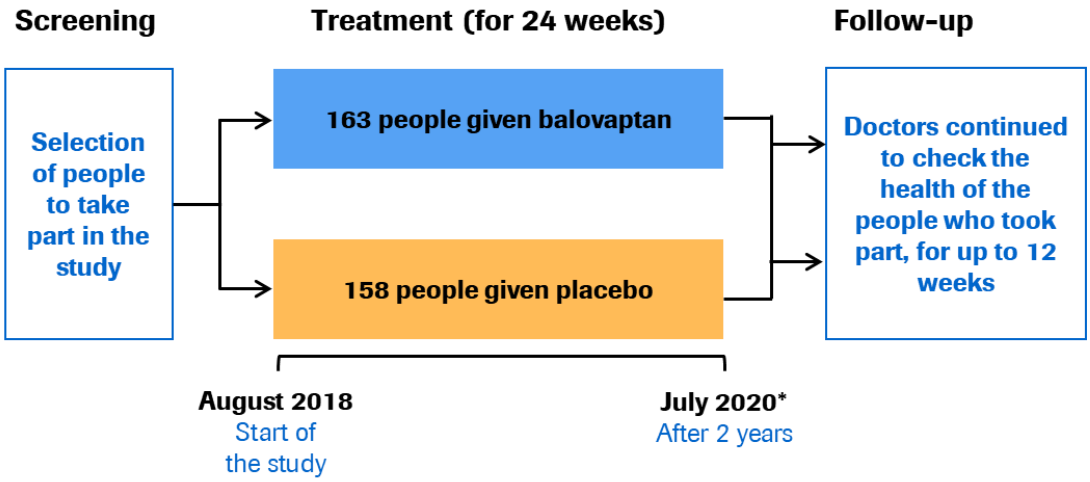
- They were pregnant, breastfeeding, or planning to get pregnant.
- They had specific conditions, such as heart problems that might affect their participation in the study.

3. What happened during the study?

During the study, people were selected randomly, by a computer, to get either balovaptan or a placebo.

The two treatment groups were:

- **Balovaptan** (the medicine being studied) was taken by mouth once every day for 24 weeks.
- **Placebo** was taken by mouth once every day for 24 weeks.



*The study was stopped early when approximately half of the people participating in the study reached Week 24 and researchers determined that the medicine did not work as well as expected. Some people who took balovaptan (and not a placebo) during the study had chosen to continue taking balovaptan after Week 24, and some people who took placebo during the study had started to take balovaptan after Week 24 – this is called an open-label extension. However, when the study ended early, the people taking part in the open-label extension had to stop taking balovaptan too.

4. What were the results of the study?

Question 1: Can balovaptan improve socialisation and communication in people with autism?

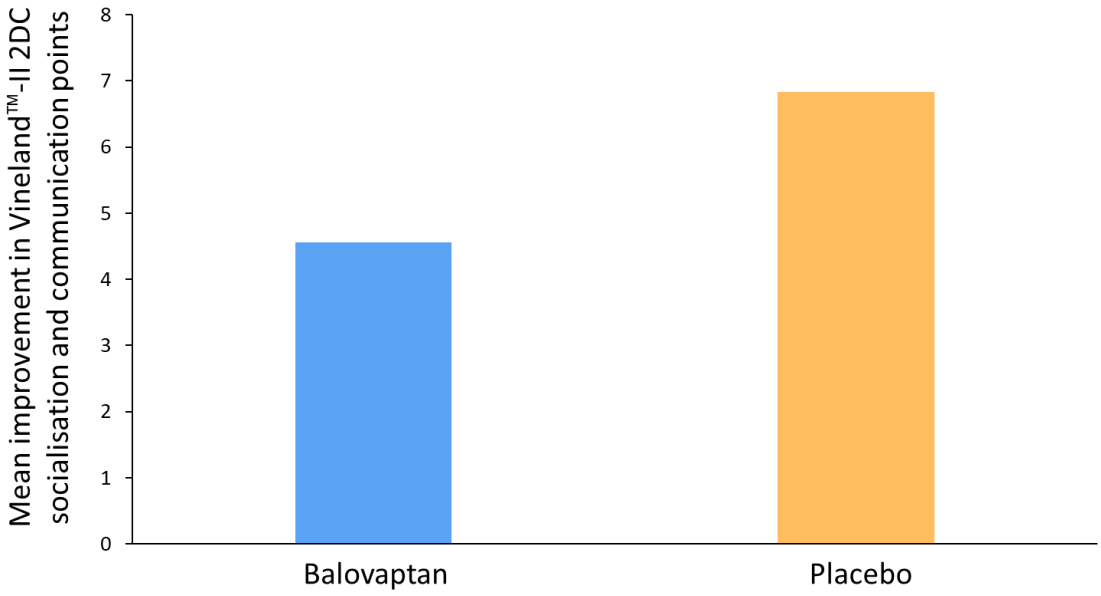
Researchers looked at people's socialisation and communication skills at the start of the study and after 24 weeks.

- Socialisation skills include how well a person interacts with others, how they play and use leisure time, and their coping skills.

- Communication skills include how well a person understands language, how they use words and sentences, and their writing skills.
- People who were given balovaptan and people who were given a placebo had improved socialisation and communication skills after around 24 weeks.
- People who were given balovaptan did not improve more than those who were given a placebo, indicating that balovaptan did not work better than placebo in this group of adults with autism.

The graph below shows the mean improvement in socialisation and communication skills for people taking balovaptan or placebo at 24 weeks, compared with at the start of the study.

- Socialisation and communication skills were measured by the Vineland™-II two-domain composite (2DC) score* – an improvement in points on this score means that there was an improvement in socialisation and communication.
- People who took balovaptan improved by 4.56 points and people taking placebo improved by 6.83 points.
- The difference in improvement between people who were given balovaptan and people who were given placebo was not meaningful and might have happened by chance.



*The Vineland™-II 2DC score assesses socialisation and communication skills of the autistic person – it is a semi-structured interview where a doctor asks the caregiver questions about the autistic person.

This section only shows the key results from this study. You can find information about all other results on the websites listed at the end of this summary (see Section 8 "Where can I find more information?").

5. What were the side effects?

Side effects are unwanted medical problems (such as feeling dizzy) that happen during a study.

- They are described in this summary because the study doctor believed the side effects could be related to the treatments in the study.
- Not all of the people in this study had all of the side effects and some people had no side effects at all.
- Side effects may be mild to very serious. How people experience side effects can vary.
- It is important to be aware that the side effects reported here are from this specific study. Therefore, the side effects described here may be different from those seen in other studies.
- Serious and common side effects for this study are listed in the sections below.

Serious side effects

A side effect is considered 'serious' if it is life-threatening, needs hospital care, or causes lasting problems.

During this study, no people who took balovaptan or a placebo had serious side effects.

During the study, some people decided to stop taking their medicine because of side effects:

- For people taking balovaptan, 2 out of 163 people (1%) stopped taking their medicine.
- In the placebo group, 2 out of 158 people (1%) stopped taking their medicine.

Most common side effects

During this study, around 17 out of every 100 people (17%) had a side effect that was not considered serious. Around 17% of people taking balovaptan had a side effect that was not considered serious, compared with around 16% of people taking a placebo.

The five most common side effects for people who took balovaptan or a placebo are shown in the table here. Some people had more than one side effect – this means that they are included in more than one row in the table.

Most common side effects reported in this study	People taking balovaptan (163 people total)	People taking placebo (158 people total)
Feeling tired	2% (4 out of 163)	2% (3 out of 158)
Feeling sleepy/drowsy	2% (3 out of 163)	1% (2 out of 158)
Feeling dizzy	Less than 1% (1 out of 163)	2% (3 out of 158)
Feeling sick	1% (2 out of 163)	1% (2 out of 158)
Increased appetite	2% (3 out of 163)	Less than 1% (1 out of 158)

Other side effects

You can find information about other side effects (not shown in the sections above) on the websites listed at the end of this summary – see Section 8.

6. How has this study helped research?

In this study, socialisation and communication improved in both balovaptan and placebo groups, so the improvements were not related to the medicine balovaptan. There were no serious side effects observed in either the balovaptan or in the placebo group.

The information presented here is from a single study of 322 people with autism (322 people took part, but only 321 people received balovaptan or placebo due to the study being stopped early). These results helped researchers and the autism community learn more about socialisation and communication difficulties in autism and about the effect of balovaptan.

Although there was no medicine-related improvement in socialisation and communication after 50 out of every 100 people (50%) completed Week 24, it was very valuable for researchers to collect this information to learn more about balovaptan and about autism.

No single study can tell us everything about the risks and benefits of a medicine. It takes lots of people in many studies to find out everything we need to know. The results from this study may be different from other studies that include the same medicine, such as the previous VANILLA trial of balovaptan in adults with autism.

- **This means that you should not make decisions based on this one summary – always speak to your doctor before making any decisions about your treatment.**

7. Are there plans for other studies?

At the time of writing this summary, no more studies looking at balovaptan for the treatment of autism are planned.

8. Where can I find more information?

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

- https://clinicaltrials.gov/ct2/show/results/NCT03504917
- https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-004378-32/results
- https://forpatients.roche.com/en/trials/neurodevelopmental-disorder/autism-spectrum-disorder/a-study-of-balovaptan-in-adults-with-autism-spectrum-disorder-wi.html

If you would like to find out more about the results of this study, the full title of the relevant scientific paper is: "Efficacy and safety of balovaptan for socialisation and communication difficulties in autistic adults in North America and Europe: a phase 3, randomised, placebo-controlled trial". The authors of the scientific paper are: Suma Jacob, Jeremy Veenstra-Vanderweele, Declan Murphy, James McCracken, and others. The paper is published in the journal 'The Lancet Psychiatry', *https://doi.org/10.1016/S2215-0366(21)00429-6*.

Who can I contact if I have questions about this study?

If you have any further questions after reading this summary:

- Visit the ForPatients platform and fill out the contact form – https://forpatients.roche.com/en/trials/neurodevelopmental-disorder/autism-spectrum-disorder/a-study-of-balovaptan-in-adults-with-autism-spectrum-disorder-wi.html
- Contact a representative at your local Roche office.

If you took part in this study and have any questions about the results:

- Speak with the study doctor or staff at the study hospital or clinic.

If you have questions about your own treatment:

- Speak to the doctor in charge of your treatment.

Who organised and paid for this study?

This study was organised and paid for by F. Hoffmann-La Roche Ltd who have their headquarters in Basel, Switzerland.

Full title of the study and other identifying information

The full title of this study is: “Efficacy and safety of balovaptan for socialisation and communication difficulties in autistic adults in North America and Europe: a phase 3, randomised, placebo-controlled trial”.

The study is known as ‘V1aduct’.

- The protocol number for this study is: WN39434.
- The ClinicalTrials.gov identifier for this study is: NCT03504917.
- The EudraCT number for this study is: 2017-004378-32.