Results from the PASADENA study: prasinezumab treatment for early-stage Parkinson's disease over 2 years

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 June 2017 and this summary includes the complete results that were collected until September 2021. At the time of writing this summary, this study is still ongoing – this summary presents the complete results for parts one and two of the study. This summary will be updated when the study ends.

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.**

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Glossary

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Thank you to the people who took part in this study

The people who took part have helped researchers to answer important questions about **Parkinson's Disease (PD)** and the medicine studied – 'Prasinesumab'.

Date of preparation: August 2022, revised on April 2023 M-XX-00010353

Summary

The purpose of this study was to see whether the medicine under investigation, “prasinezumab”, was well-tolerated and if it could slow the speed at which Parkinson’s disease (PD) worsens in people with early-stage PD.

One year of treatment with prasinezumab did not slow the overall worsening of the disease; however, this study showed that prasinezumab was well tolerated and reduced the worsening of motor signs (movement-related) in participants with early-stage PD. It also showed that PD motor signs progressed at a slower rate when study participants were treated with prasinezumab for 2 years than when participants received prasinezumab for 1 year only. Based on these results, Roche has started a new study called PADOVA, to continue investigating the potential of prasinezumab to slow down the worsening of PD.

1. Key information about this study

What is this summary about?

This is a plain language summary of an article originally published in The New England Journal of Medicine (see here for the article: Pagano G, et al. 2022). It is about the results from the first two parts of the three-part PASADENA clinical trial (study), which looked at the potential of a new treatment called prasinezumab to slow the speed at which **Parkinson’s disease (PD)** worsens.

There are currently no treatments available that slow down the progression of PD or stop brain cells from dying. Prasinezumab has been designed to target a protein in the brain called alpha-synuclein. It is thought that in PD, alpha-synuclein does not form properly and clumps together, damaging brain cells. Prasinezumab may stop these clumps from forming and, therefore, may reduce the rate at which brain cells are damaged or die.

What happened in the PASADENA study?

In the PASADENA study, researchers wanted to find out if treatment with a low or high dose of prasinezumab could slow the speed at which PD worsened when compared with **placebo**. In total, 316 participants with early-stage PD were split into three groups: a high-dose prasinezumab group, a low-dose prasinezumab group and a placebo group.

The PASADENA study is divided into three parts: Part 1 – 52 weeks (1 year) of treatment, Part 2 – 104 weeks (2 years) of treatment and Part 3 – 5 years of treatment. As of August 2022, Part 3 of the study is still ongoing; in this summary, the results of Parts 1 and 2 are shown below.

Over the course of the study, participants were assessed regularly to find out if there was

any worsening in their movement (motor symptoms and signs) and other symptoms (non-motor symptoms).

What were the results?

After 1 year of treatment, researchers could not see a **statistically significant** difference between participants who took prasinezumab and those who took placebo when looking at the overall disabilities and symptoms (motor and non-motor). However, when looking at only the motor signs, those taking prasinezumab appeared to worsen less than the placebo group.

After 2 years of treatment, researchers found that participants who had taken prasinezumab (low or high dose) for 2 years continued to show a slower worsening in motor signs compared with those who were taking placebo at first and then started taking prasinezumab at 52 weeks. The slowing of worsening was similar between those who received low dose and those who received high dose prasinezumab.

What do the results of the study mean?

The main result of this study was that prasinezumab did not slow the overall progression of PD, but that prasinezumab was well tolerated and slowed the worsening of motor signs in participants with early-stage PD.

Part 3 of this study is on-going and further analysis will be done to understand the effect of prasinezumab in people with early-stage PD. Based on the PASADENA results, in a new study called PADOVA, Roche is pursuing further research into the potential of prasinezumab to slow down the worsening of PD.

Who sponsored this study?

This study was funded by F. Hoffmann-La Roche Ltd and Prothena Biosciences Ltd, and they are the first companies to use this specific molecule for the treatment of PD progression.

Thank you to all the participants and their family and friends who took part in this study

The people who took part in this study have helped researchers answer important questions about PD and prasinezumab.

2. General information about this study

What was the aim of this study?

PD is estimated to affect over 10 million people worldwide (Parkinson's Foundation). There are currently no treatments that prevent or slow the worsening of this disease.

Current PD treatments help to manage the early effects of the disease on movement, mainly using medicines that replace **dopamine**, a chemical in the brain that is lacking in people with PD due to the loss of brain cells. However, despite the symptom relief brought by current treatments, this does not reverse, slow down or stop brain cells from dying, so as the disease gets worse, these medicines become less effective at controlling the symptoms.

Researchers are testing new medicines that can prevent brain cell death in order to stop or slow the speed at which PD gets worse. Prasinezumab is one of these medicines.

What was the medicine being studied?

Prasinezumab is the drug being investigated in this study. It is an antibody that has been designed to bind to alpha (α)-synuclein and slow PD progression.

α-synuclein is a protein that is naturally present in the brain. It is normally found inside brain cells, at the ends of the cells where chemical messengers are released to allow communication between cells. Scientists do not yet fully understand what α-synuclein does, but it is thought to be involved in the release of dopamine and may therefore be important in movement control.

Normally α-synuclein has a spiral shape, but in PD, the protein does not form properly and clumps together. These clumps are found in the brains of individuals with PD, when examined post-mortem. They may be toxic and cause brain cells to die. Sometimes, clumps are able to exit the cell they were produced in and enter neighbouring brain cells. When this happens, it causes neighbouring cells to die and PD to worsen.

Prasinezumab is an antibody that binds to these toxic clumps of α-synuclein and may stop the clumps from damaging brain cells. This may help to slow the worsening of PD.

Prasinezumab is an injectable drug: it is a liquid solution injected into a vein (known as an **intravenous** or IV injection).

What is the PASADENA study?

PASADENA is an acronym for The **P**hase II trial of **A**nti alpha-**S**ynuclein **A**ntibo**D**y in **E**arly Parki**N**son's dise**A**se

PASADENA is a clinical trial (study) has started in 2017 and is ongoing. Its purpose is to assess if prasinezumab, a new medicine, could slow the speed at which PD worsens.

The PASADENA study is made up of three parts (see Figure 1 and Figure 2):

- **Part 1**

At the start of the study, 316 participants with early-stage PD were divided into **three groups** and were monitored for 52 weeks (1 year):

– **Group 1 – Placebo:** 105 participants received a placebo (a non-active substance). A placebo looks the same as the study medicine but does not contain any real medicine

– **Group 2 – Low-dose prasinezumab:** 105 participants received a dose of 1500 mg of prasinezumab (referred to as the low-dose study group)

– **Group 3 – High-dose prasinezumab:** 106 participants received a dose of 4500 mg of prasinezumab (referred to as the high-dose study group).

Part 1 of the study was carried out between June 2017 and November 2019. This part of the study was completed after all participants received prasinezumab or placebo for 52 weeks and completed their 1-year visit.

- **Part 2**

The second part of the study was also 52 weeks (1 year) long. In total, 309 participants who took part in Part 1 continued into Part 2 of this study.

Participants who received placebo in Part 1 joined either the low-dose (1500 mg) or the high-dose (4500 mg) prasinezumab study group in Part 2. This group is referred to as the **delayed-start group,** since they received prasinezumab only, after the end of Part 1.

All participants who received prasinezumab (high or low dose) since the beginning of the study are referred to as the **early-start group.**

Part 2 consisted of two study groups:

– **low-dose prasinezumab:** 152 participants received a low (1500 mg) dose of prasinezumab: this included 100 participants who had already received a low dose of prasinezumab in Part 1 and 52 participants who received the placebo in Part 1

– **high-dose prasinezumab:** 157 participants received a high (4500 mg) dose of prasinezumab: this included 104 participants who had already received a high dose of prasinezumab during Part 1 and 53 participants who received placebo in Part 1.

Part 2 of the study was completed in November 2020, after all Part 2 participants attended their 2-year (104 weeks) visit.

- **Part 3**

Part 3 is a 5-year (260 week) extension of the study with all participants receiving a low dose of prasinezumab (1500mg). It started in August 2020 and will be completed in September 2026. The purpose of this part of the study is to assess if prasinezumab is able to slow PD progression and how it is tolerated in the long term.

Figure 1. PASADENA study design

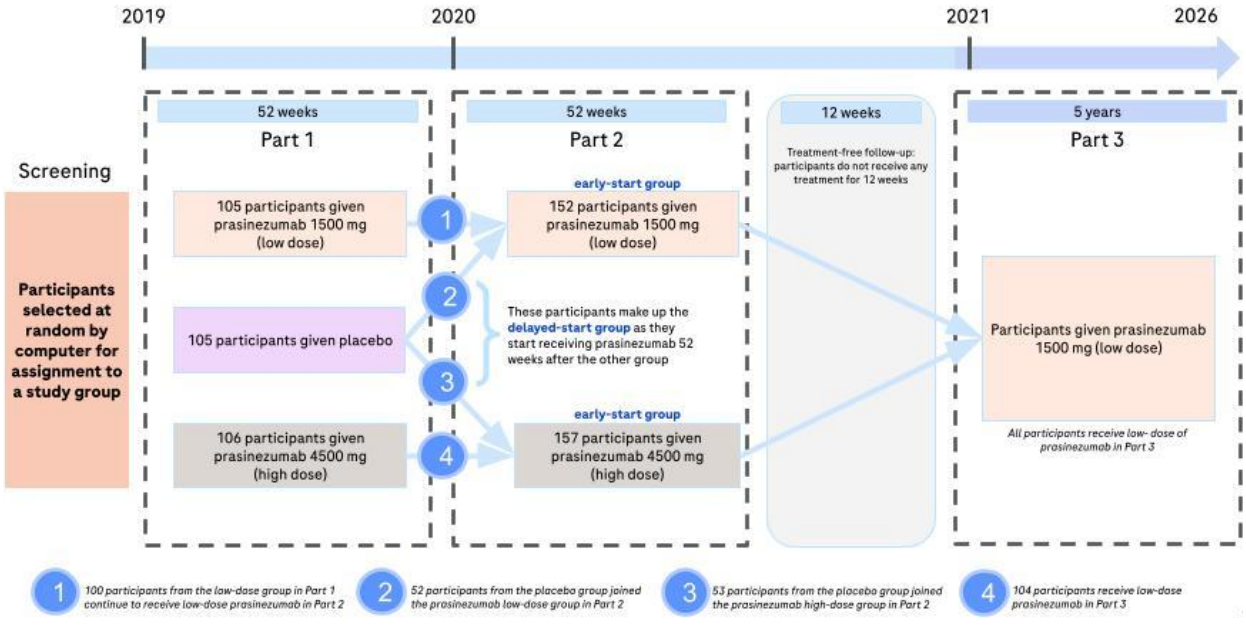
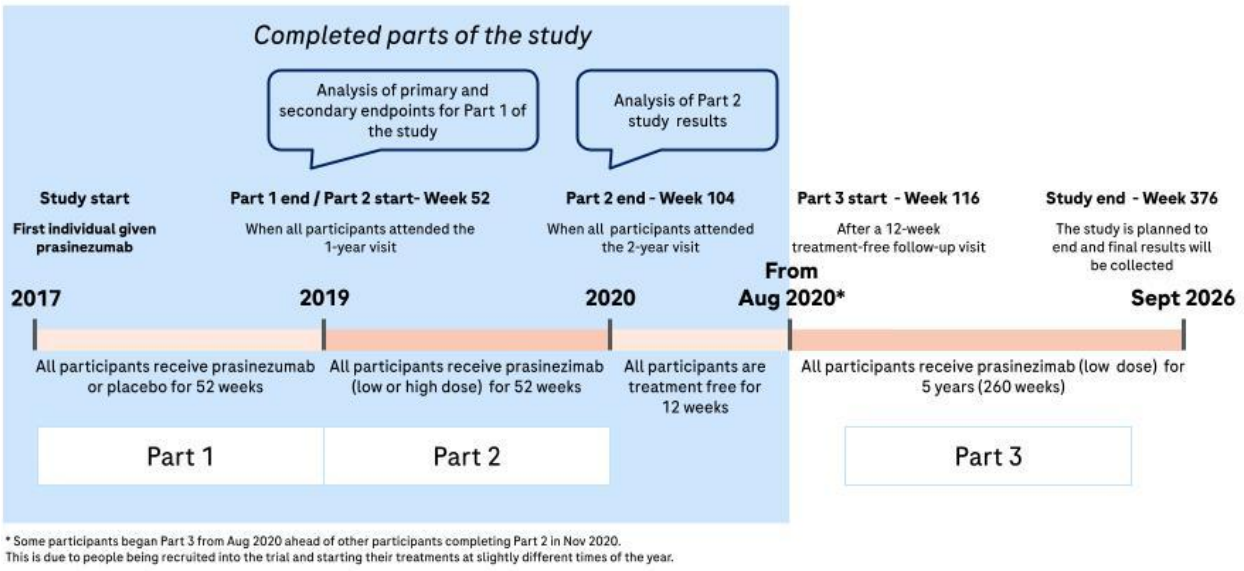


Figure 2. PASADENA study timelines



What kind of study was this?

The PASADENA study is a Phase II study. Before this Phase II study, prasinezumab has been tested in three Phase I studies:

- Two Phase I studies in healthy volunteers to ensure that prasinezumab could be used safely in humans.
- A Phase I study with participants with early-stage PD to ensure that prasinezumab could be used safely in this population.

The study participants in PASADENA were **randomised**. This means that it was decided by chance who would be given prasinezumab and who would be given placebo – like tossing a coin. Randomly choosing whether someone gets placebo or medicine makes it more likely that the types of people in both groups (for example, sex, age, ethnicity) will be a similar mix. Apart

from the medicines being tested in each group, all other aspects of care were the same between the groups.

This is a double-blind study. This means that neither people taking part in the study, nor the researchers (neurologists) knew if participants were receiving prasinezumab or placebo.

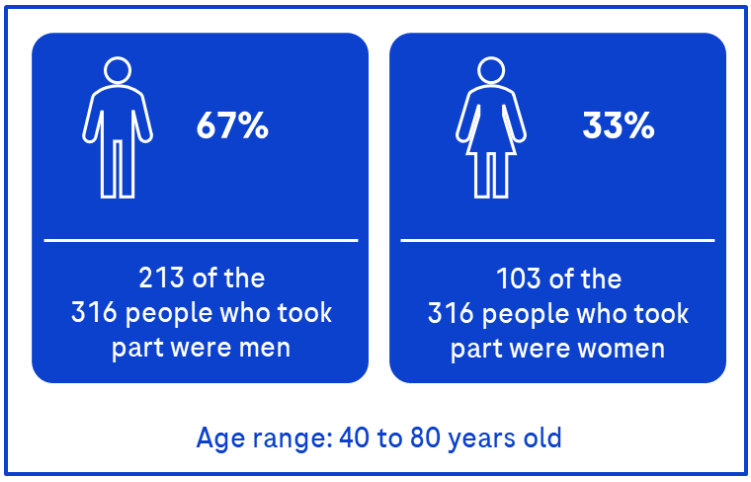
A '**placebo**' looks exactly the same as a medicine but does not contain any real medicine. A placebo is used so that participants and the researcher (neurologist) do not know who is receiving the real medicine. This is because sometimes just knowing you are taking a treatment that might help you can cause small improvements in a condition, which affects the results of the study.

'Blinding' of a study is done so that any effect seen from the study medicine is real and not exaggerated due to the participant's or researcher's expectations of the effects of a study medicine. This is particularly important when the effects of the medicine are being evaluated by tests and examinations that are completed by a researcher's trained judgement.

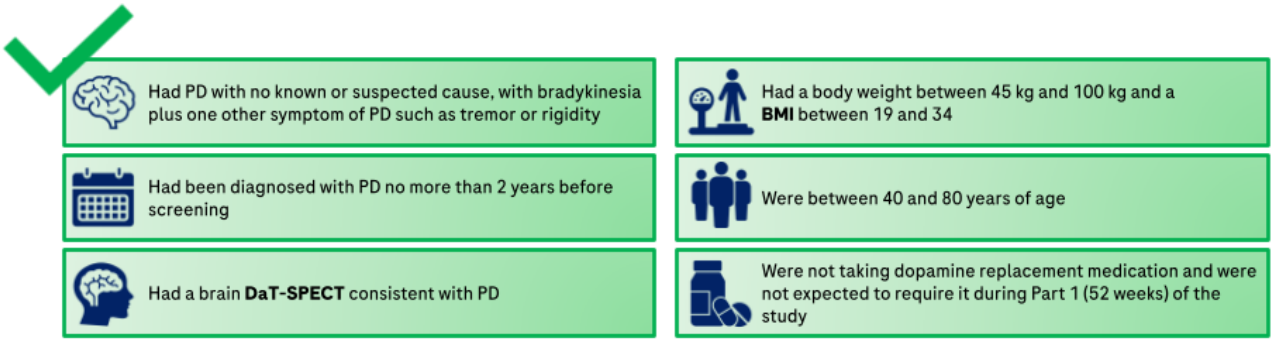
* If you would like to learn more about clinical studies, please see:
https://clinicaltrials.gov/ct2/about-studies/learn#WhatIs

3. Who took part in this study?

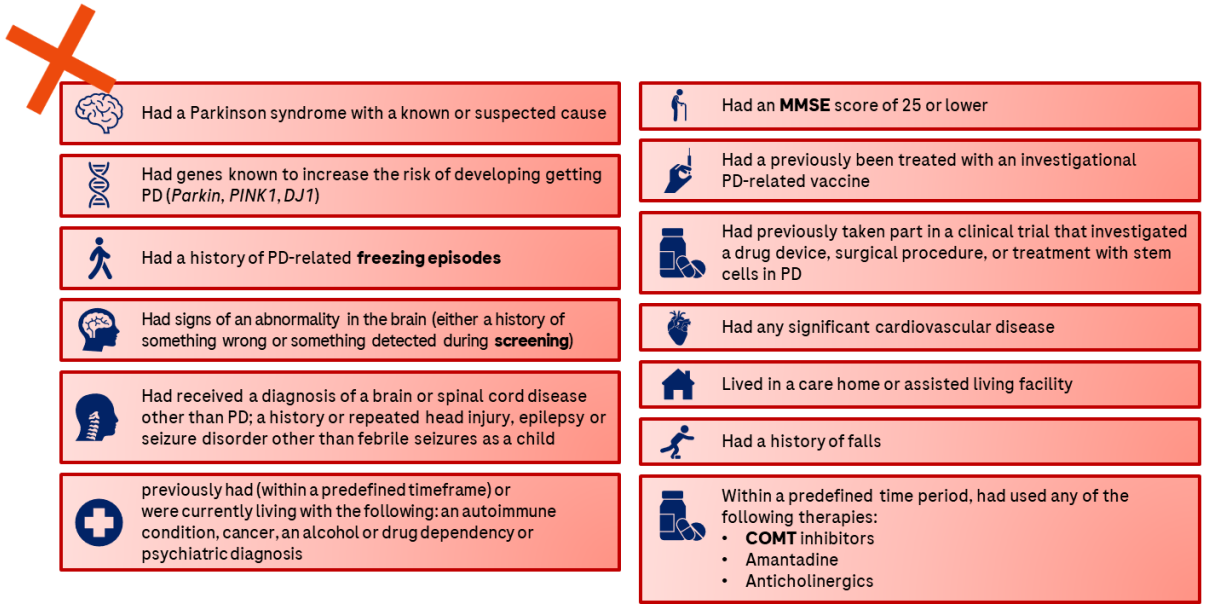
At the start, this study included 316 participants (**Part 1** of the study). Two hundred and thirteen participants (67%) were men and 103 participants (33%) were women. They were all 40–80 years of age. Out of these 316 people, 309 continued to **Part 2**.



People could take part in the study if they:



People could **not** take part in the study if they:



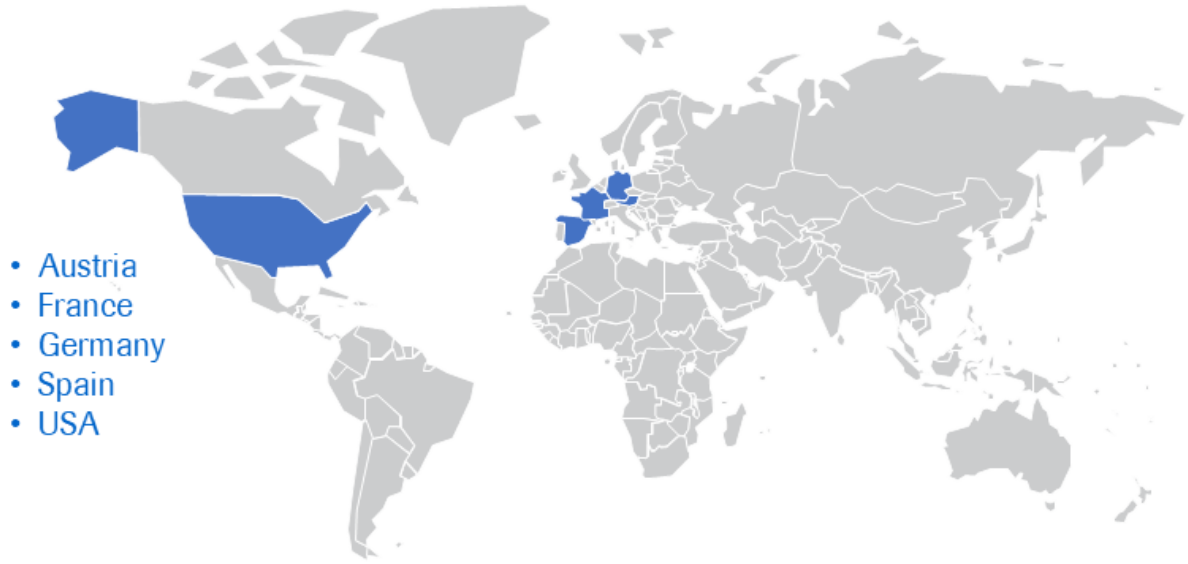
BMI, body mass index; **COMT**, catechol-O-methyltransferase; **DaT-SPECT**, dopamine transporter imaging with single-photon emission computed tomography; **MMSE**, Mini Mental State Examination; **PD**, Parkinson's disease.

These criteria made sure that the people taking part in the study were as similar as possible and to exclude other medications or medical conditions that would have made the results difficult to compare.

For more information on who could and could not take part in the PASADENA study, please see: https://clinicaltrials.gov/ct2/show/results/NCT03100149

Where did the study take place?

The study took place at 57 hospitals across Austria, France, Germany, Spain and the USA.



4. What happened during the study?

How were the effects of prasinezumab on PD assessed in this study?

To understand the results of the PASADENA study, it is first important to understand the features of PD, and the signs and symptoms that are important to measure in order to determine if the disease is progressing. Understanding this will allow us to accurately assess if the studied medicine does have an impact on PD progression.

What are the signs and symptoms of PD?

PD is a slow, long-term brain condition that gets worse over time. PD develops when brain cells that produce the chemical dopamine die. Dopamine is a key chemical 'messenger' in the brain and contributes to our ability to process information.

Dopamine is also needed in the brain to control movement – when brain cells start to die, a person with PD cannot make enough dopamine to control their movement properly and begins to show movement-related symptoms such as **resting tremor**, **rigidity** or **bradykinesia** (slowness of movement and reduced amplitude [range or extent of movement] or speed of movement).

The drop in dopamine levels also causes a range of symptoms that are not movement related (also called 'non-motor symptoms'), including constipation, sleep problems and cognitive problems (e.g. changes in thinking, understanding, remembering and problem-solving; dementia; visual hallucinations; anxiety; depression; or fatigue). These symptoms are often subtle and can start to appear many years before changes in movement are noticed.

PD develops very slowly and many of the movement and non-movement related symptoms are not obvious until the disease is well advanced, making them difficult to measure.

As more and more dopamine-producing cells die over time, PD symptoms worsen, and people need to receive dopamine-replacement therapy (also known as symptomatic therapy) to help relieve their symptoms.

How can the worsening of PD be measured?

There is no specific test to diagnose or assess how PD worsens over time. Neurologists assess the signs and symptoms of PD using neurological and physical examinations.

MDS-UPDRS questionnaire

The **MDS-UPDRS** (Movement Disorder Society-Unified Parkinson's Disease Rating Scale) is a questionnaire developed by neurologists who have expertise in PD, to evaluate the burden of disease and various aspects of PD including motor and non-motor symptoms and signs, and motor complications, and the impact PD has on an individual's daily life.

The MDS-UPDRS questionnaire is the main tool used by neurologists to measure the severity and progression of PD.
It consists of 50 questions divided into **four sections (Figure 3)**:

- **Part I – non-motor experiences of daily living:** This section is completed by people with PD. They need to answer questions related to their non-motor experiences of daily living over the last 7 days (e.g. sleep and mood problems, pain). It is divided into two subsections:

  - **Part Ia:** Asks people with PD about examples of behaviours that might be symptoms of their disease, such as their cognitive symptoms (ability to process information and problems with memory), mood symptoms (depression and anxiety), impulsive behaviour (gambling, addictive or repetitive behaviours) and hallucinations (seeing/hearing/smelling things that are not there). For each person, the researcher decides on a score from 0–4 depending on the person's response

  - **Part Ib:** This section of the questionnaire asks people about examples of physical symptoms of PD, such as pain, bladder problems, constipation, light-headedness and fatigue. The researcher decides on a score from 0–4 depending on the person's response.

- **Part II – motor experiences of daily living**: This section is a questionnaire completed by people with PD. Questions are related to motor experiences of daily living over the last 7 days with people able to report problems related to movement such as speaking, eating (chewing and swallowing), using a knife and fork, dressing, washing, writing and everyday movements such as turning in bed, getting out of a chair and walking/balance. Depending on how the individual answers, the researcher will give a score from 0–4.

- **Part III – motor examination:** A physical examination carried out by the neurologist to assess movement (called motor signs of PD). It is a "rate what you see" examination by the neurologist who looks at the person's speech, facial expression, rigidity, bradykinesia and resting tremor.

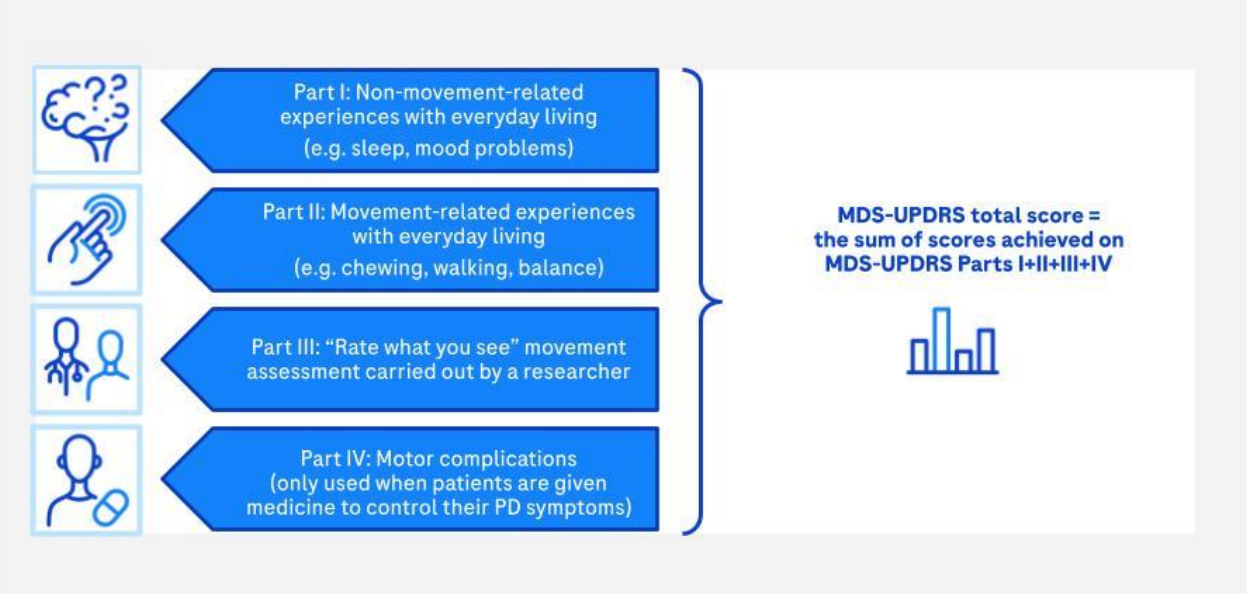
- **Part IV – motor complications:** The assessment of motor complications is used to assess individuals at advanced disease stages. This assessment is performed when people are given medicine to control their PD symptoms (dopamine-replacement therapy).

The MDS-UPDRS total score is the addition of the scores obtained in the different sections of the questionnaire and examination. A higher score means that the symptoms and the disease progression are worse.

The MDS-UPDRS total score for each study participant is the addition of the available subscores they obtained on MDS-UPDRS Parts I, II and III and part IV.

For more information on the MDS-UPDRS assessment scale please see: https://www.movementdisorders.org/MDS-Files1/PDFs/Rating-Scales/MDS-UPDRS_English_FINAL_Updated_August2019.pdf

Figure 3. The MDS-UPDRS is used to assess PD signs and symptoms and how they worsen over time. In the PASADENA study, information for MDS-UPDRS Parts I, II and III is being collected from the study start. MDS-UPDRS Part IV is studied only when the participants have started dopamine-replacement therapy in the advanced stages of PD.



MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale.

How were the effects of prasinezumab on PD assessed in this study?

The study participants were asked to complete the MDS-UPDRS questionnaire every 8 weeks. This allowed researchers to calculate the change in MDS-UPDRS total score over time as a way of assessing if PD symptoms and signs worsened over the course of the study and also find out

if they worsened more or less in the prasinezumab-treated group compared with the placebo group.

The main question (also known as the primary endpoint) that researchers wanted to answer in Part 1 of this study was:

Question 1:

Does 1 year (52 weeks) of treatment with prasinezumab slow the worsening of overall PD progression?

This question was answered by comparing, after 1 year, the MDS-UPDRS total score (sum of MDS-UPDRS scores for Parts I+II+III) between the study groups (placebo and prasinezumab low- and high-dose groups).
A study participant who had an increase of at least 5 points in their MDS-UPDRS total score was considered to have a worsening of symptoms.

Other important questions (known as the secondary and exploratory endpoints) that researchers wanted to answer in Part 1 of this study were:

Question 2:

Does 1 year (52 weeks) of treatment with prasinezumab slow the progression of some specific PD symptoms and signs?

This question was answered by comparing score changes on the individual sections of the MDS-UPDRS:

- **non-movement-related symptoms:** by comparing MDS-UPDRS Part Ia and Part Ib scores between the three study groups (placebo and low- and high-dose prasinezumab)
- **movement-related symptoms:** by comparing MDS-UPDRS Part II scores between the study groups
- **clinical signs of PD as observed by the neurologist:** by comparing MDS-UPDRS Part III scores between the study groups.

Question 3:

How long does it take before symptoms and signs get worse?

The worsening of the symptoms and progression of PD is reflected by a change (at least 5 points) in the MDS-UPDRS total score (sum of MDS-UPDRS scores for Part Ia, Ib, II and III).

Question 4:

How long did it take for the participants to begin dopamine-replacement therapy?

A neurologist will prescribe dopamine-replacement therapy when a person's quality of life is affected, and they are in need of medicine to relieve movement-related symptoms. The time to start dopamine-replacement therapy is a measure of disease progression.

The questions the researchers wanted to answer in Part 2 (at Week 104) of the study were:

Question 5:

Was there a difference in overall disease progression between:

- Participants who took prasinezumab for 2 years (early-start study group: participants who received prasinezumab in Part 1 and Part 2 of the study)
- and participants who took prasinezumab for 1 year (delayed-start study group: participants who received the placebo in Part 1 and prasinezumab in Part 2)?

This question is answered by comparing, after 2 years, the change in MDS-UPDRS total score (Parts I+II+III) between the early-start and the delayed-start groups.

Question 6:

Was there a difference in PD motor signs evaluated by the neurologist between:

- Participants who took prasinezumab for 2 years (early-start study group: participants who received prasinezumab in Part 1 and Part 2 of the study)
- and participants who took prasinezumab for 1 year (delayed-start study group: participants who received the placebo in Part 1 and prasinezumab in Part 2)?

This question is answered by comparing, after 2 years, the MDS-UPDRS Part III score between the early-start and the delayed-start groups.

5. What were the results of the study?

To conclude if prasinezumab can slow the worsening of PD symptoms and signs, it is important to understand if the results seen in the study are really due to the effect of prasinezumab and not due to chance or randomness.

Researchers do this by determining if the results are **statistically significant.** When a finding is statistically significant, it means that the researchers are confident that the result observed is real and not due to chance.

If a result is found to be not statistically significant, it is not possible to conclude if the drug is having a real effect on symptoms as any changes seen might be due to chance.

What were the results of the study after 1 year (Part 1 of PASADENA)?

Question 1:

Was there any difference overall in how symptoms and signs of PD changed in participants after 52 weeks of being treated with either prasinezumab or placebo?

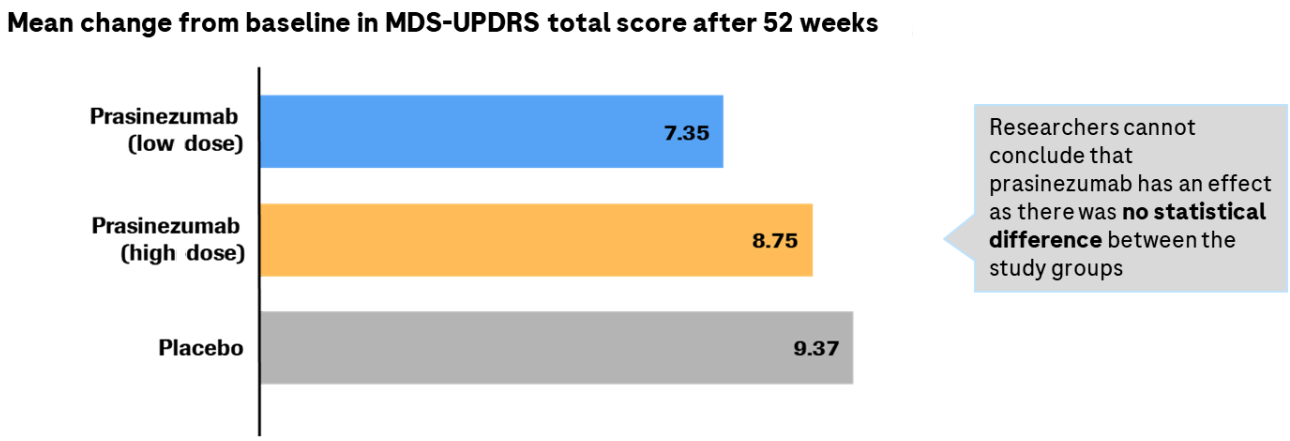
After 52 weeks (1 year), there was no overall difference in MDS-UPDRS total score (sum of Parts I+II+III) between participants who took prasinezumab (high or low dose) and participants who took placebo.

That means when compared with their symptoms and signs at the study start (called baseline level), participants who received high-dose prasinezumab, low-dose prasinezumab or placebo had a similar worsening of their overall PD symptoms and signs (the combination of non-movement-related symptoms, movement-related symptoms and clinical signs of the disease when examined by a neurologist).

The researchers were able to conclude that prasinezumab (low or high dose) did not slow the overall progression of PD when given to participants with early-stage PD for 1 year.

A small difference in the mean (average) MDS-UPDRS total score was seen between the study groups (Figure 4), but this difference in score was **not statistically significant**. This means that this result does not show a real difference in the overall PD symptoms between the study groups.

Figure 4. PASADENA study Part 1 (52 weeks). Mean MDS-UPDRS total score (sum of Parts I+II+III scores)



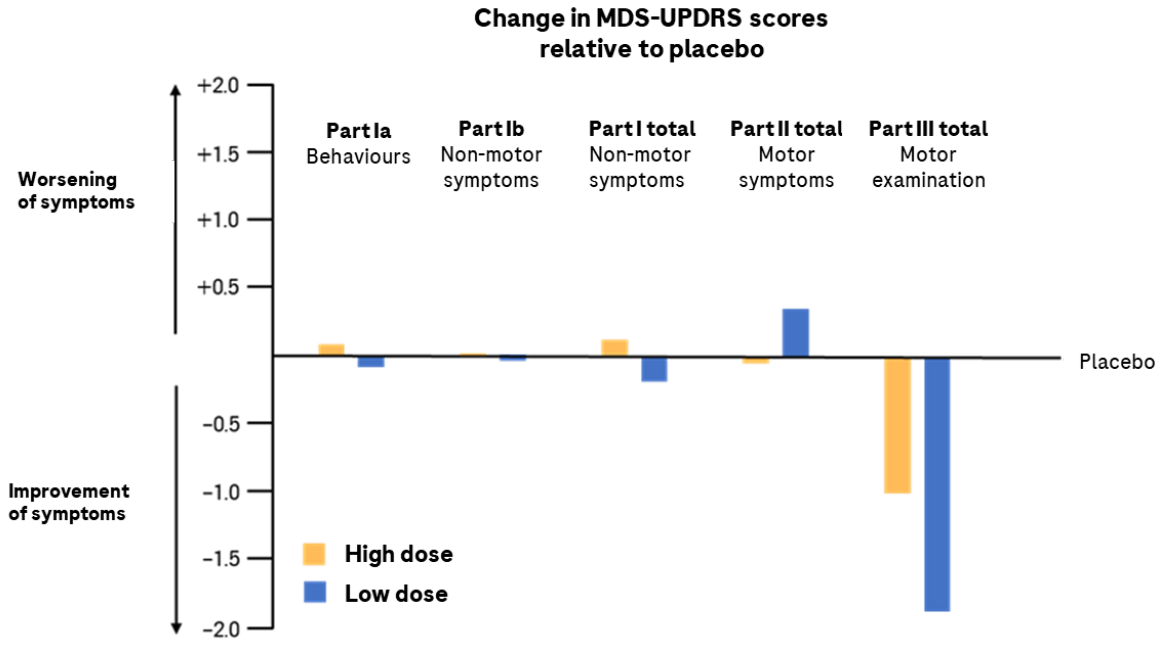
Higher scores indicate increased worsening compared with the start of the study.
MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale.

Question 2:

Does 1 year (52 weeks) of treatment with prasinezumab slow the progression of some specific PD symptoms and signs?

Yes, participants receiving prasinezumab for 1 year had a more favourable motor examination than participants receiving placebo (Figures 5 and 6).

Figure 5. PASADENA study Part 1 (52 weeks). Individual sections of the MDS-UPDRS



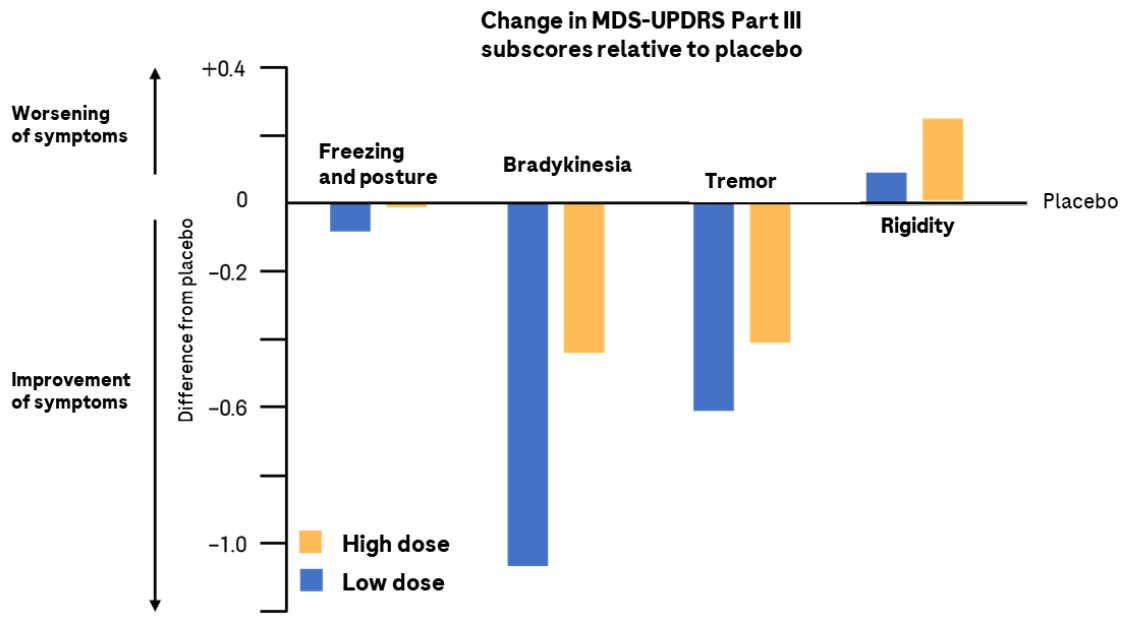
Differences between the high dose and low dose prasinzumab groups were not significant.
MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale.

There was no significant difference between the low and high dose of prasinezumab as both doses demonstrated similar effects. Although there appears to be some small differences in the bars shown in figure 5, the differences between the low and high dose groups were not significant and therefore researchers can conclude that both doses were having a similar effect.

When looking at the details of the motor examination (the MDS-UPDRS Part III subscore), participants receiving prasinezumab (high and low dose) showed an improvement in bradykinesia and in resting tremor compared with the participants who received placebo (Figure 6).
No difference was seen between the low- and high-dose prasinezumab groups.

It is important to note that bradykinesia is often the first motor sign people with PD experience, and it tends to worsen at a faster rate than other motor signs.

Figure 6. PASADENA study Part 1 (52 weeks). MDS-UPDRS Part III subscores



Differences between the high dose and low dose prasinezumab groups were not significant. Both dose groups showed a similar improvement in bradykinesia and tremor compared with placebo.
MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale.

The researchers could conclude that 1 year of treatment with prasinezumab slowed the progression of motor signs, and more specifically slowed the progression of bradykinesia in participants with early-stage PD.

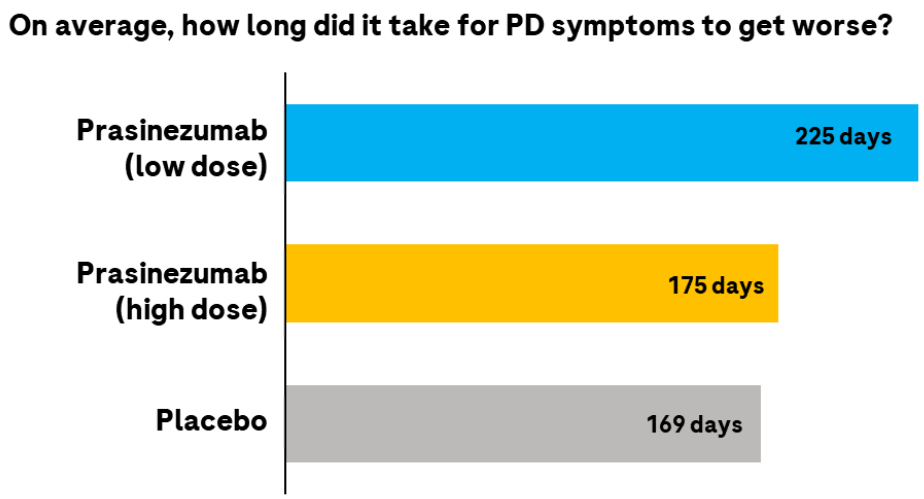
Question 3:

How long does it take before symptoms get worse?

To answer this question, researchers looked at the time it took for a participant to show an increase of at least 5 points in the MDS-UPDRS total score (Parts I+II+III).

Participants who received low dose prasinezumab had the longest time on average (225 days) until their symptoms worsened (Figure 7).

Figure 7. PASADENA study Part 1 (52 weeks). Average time to PD symptoms worsening (more than a 5 point change in the MDS-UPDRS total score [Parts I + II+III])



A longer duration indicates slower progression.
MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease.

Question 4:

How long did it take for participants to begin dopamine-replacement therapy?
Did prasinezumab increase the length of time before participants needed to start dopamine-replacement treatment?

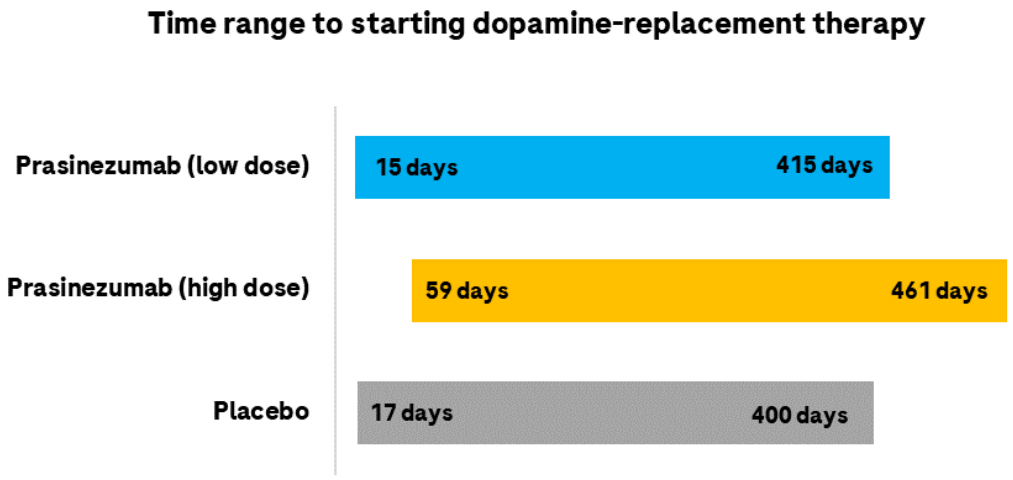
People need to start dopamine-replacement therapy when their symptoms have worsened to a point that they need to take medicine daily to help control their movements. The time to starting dopamine-replacement therapy is a way to measure the time to disease progression.

In Part 1 of the study, dopamine-replacement therapy was needed for:
- 42% of participants (44/105) in the low-dose prasinezumab group
- 34% of participants (36/106) in the high-dose prasinezumab group
- 41% of participants (43/105) in the placebo group.

The range (the difference between the shortest and longest times) for the time to starting dopamine-replacement therapy was similar in the three groups (Figure 8).

Treatment with prasinezumab did not influence the time to starting dopaminergic symptomatic therapy compared with placebo.

Figure 8. Time to starting dopamine-replacement therapy



A longer duration indicates slower progression.

What were the results of the study after 2 years (Part 2 of PASADENA)?

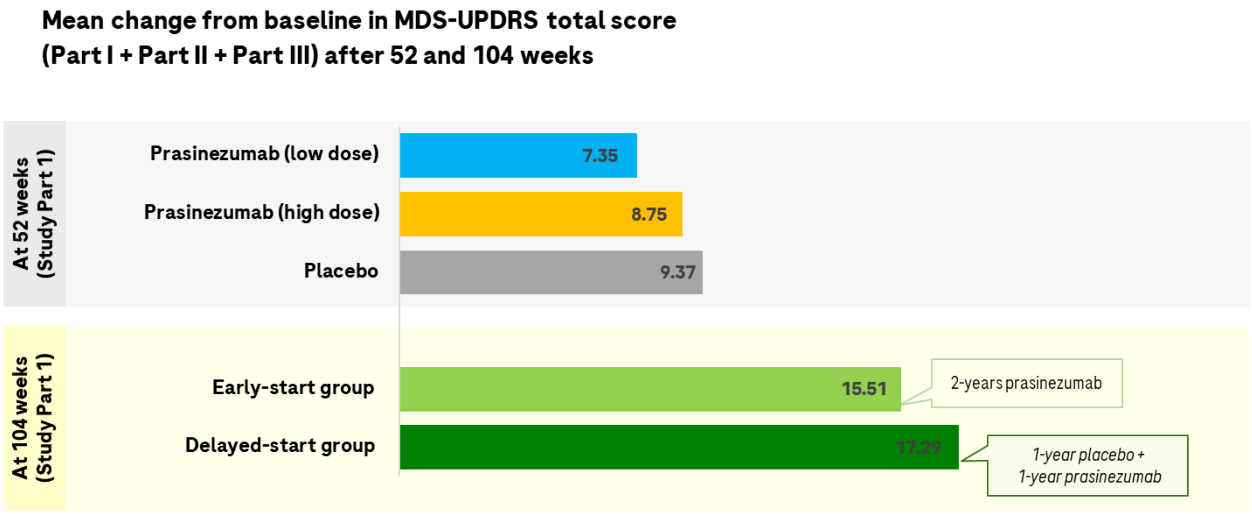
Question 5:

Was there a difference after 2 years in overall PD progression (change in MDS-UPDRS total score [Parts I+II+III]) between:

- the early-start study group: participants who received prasinezumab for 2 years
- the delayed-start study group: participants who received prasinezumab for 1 year (who received placebo in Part 1)?

After 104 weeks, no significant difference was observed between the early-start and the delayed-start groups in MDS-UPDRS total score (Figure 9).
This means that 1- or 2-year treatment with prasinezumab does not make a difference to overall PD progression.

Figure 9. Mean change from baseline in MDS-UPDRS total score (Parts I+II+III) after 52 and 104 weeks



higher scores indicate increased worsening compared with the start of the study.

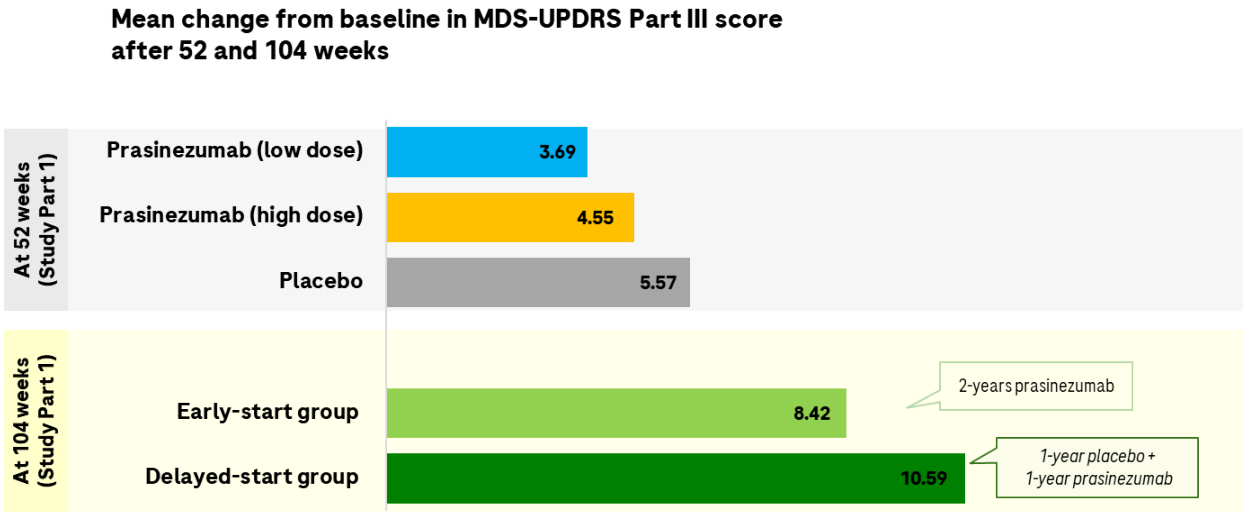
Question 6:

Was there a difference in PD motor signs evaluated by the neurologist (change in MDS-UPDRS Part III) between:

- the early-start study group: participants who received prasinezumab for 2 years
- the delayed-start study group: participants who received prasinezumab for 1 year (who received placebo in Part 1)?

Yes, after 104 weeks, the early-start group had a lower MDS-UPDRS Part III score than the delayed-start group (Figure 10).
This means that PD motor signs progressed at a slower rate when participants were treated with prasinezumab for 2-years compared with 1-year only.

Figure 10. Mean change from baseline in MDS-UPDRS Part III score after 52 and 104 weeks



higher scores indicate increased worsening compared with the start of the study.

6. What were the side effects?

What are adverse events?

An **adverse event** is a medical problem that happens during a treatment. Adverse events may be mild, moderate or serious. They may be caused by the medicine or by something other than the given medicine.

In a study, adverse events are the physical or psychological problems that participants experience during the study and are reported to the researchers.

- Not all participants in this study experienced all of the adverse events.
- It is important to be aware that adverse events reported here are from this single study. Therefore, they may be different from those seen in other studies.

When a medical problem is due to the study medicine (i.e., due to prasinezumab) or the placebo, it is called a **treatment-related adverse event or side effect.**

What are serious adverse events?

An adverse event is considered 'serious' if it is life threatening, needs hospital care, or causes lasting problems.

What adverse events occurred in this study?

In Part 1 of the study, study participants receiving low and high doses of prasinezumab experienced more adverse events than the participants receiving placebo (Table 1).

Table 1. Overview of the adverse events in Part 1 of the study

	Study Part 1 (Week 1 to Week 52)		
	Participants taking placebo (105 People)	**Participants taking low-dose prasinezumab (105 people)**	**Participants taking high-dose prasinezumab (106 people)**
Participants with at least one adverse event	82.9% (87 out of 105)	93.3% (98 out of 105)	91.5% (97 out of 106)
Serious adverse events	4.8% (5 out of 105)	6.7% (7 out of 105)	7.5% (8 out of 106)
Treatment-related adverse events	26.7% (28 out of 105)	24.8% (16 out of 105)	38.7% (41 out of 106)
Adverse events leading to stopping participation in the study	0	1% (1 out of 105)	0
Reaction related to the injection*	16.2% (17 out of 105)	19% (20 out of 105)	34% (36 out of 106)

* Reactions related to the injections were nausea and headache in the placebo group and nausea, headache and skin irritations in the prasinezumab groups (high and low dose).

In Part 1 of the study, the most common adverse events (experienced by more than 10% of the participants receiving the placebo or prasinezumab) were reactions related to the injection, flu-like symptoms, back pain and headache.

In Part 2 of the study, more serious adverse events occurred in participants who received a high dose of prasinezumab for 1 year (6 people out of 53, representing 11.3%) than in participants who received a high dose of prasinezumab for 2 years (6 people out of 104 people, representing 5.8%) (Table 2).

This difference was not seen in people receiving a low dose of prasinezumab for 1 or 2 years.

Like in Part 1, the most common adverse events were reactions to the injection and flu-like symptoms in all groups.

Two study participations were stopped during the course of Part 2, one due to illness and the other one due to death (suicide).

Table 2. Overview of the adverse events in Part 2 of the study

	Study Part 2 (Week 52 to Week 104)	
	Low-dose prasinezumab (152 people)	**High-dose prasinezumab (157 people)**
Participants with at least one adverse event	71.7% (109 out of 152)	81.5% (128 out of 157 people)
Serious adverse events	4.6% (7 out of 152)	7.6% (12 out of 157)
Treatment-related adverse events	10.5% (16 out of 152)	24.2% (38 out of 157)
Adverse events leading to stopping participation in the study	1.3% (2 out of 152)	1.3% (2 out of 157)
Reaction related to the injection	7.2% (11 out of 152)	21% (33 out of 157)

7. How has this study helped research?

The main conclusion of this study is that prasinezumab did not slow overall PD progression and that prasinezumab had a favourable safety profile. This means that overall prasinezumab was well tolerated in participants with early-stage PD.

This study showed that participants with early-stage PD treated with prasinezumab over 1 year had fewer motor signs than the placebo group. It also showed that PD motor signs progressed at a slower rate when participants were treated with prasinezumab for 2 years compared with 1 year only.

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.

8. Are there plans for other studies?

Based on these results, Roche has started a new study called PADOVA, to continue its research on prasinezumab in PD.

9. 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/NCT03100149
- https://www.clinicaltrialsregister.eu/ctr-search/search?query=2017-000087-15
  https://forpatients.roche.com/en/trials/neurodegenerative-disorder/pd/a-study-to-evaluate-the-efficacy-of-ro7046015-in-participants-wi.html
- PASADENA study design journal article:
  https://www.frontiersin.org/articles/10.3389/fneur.2021.705407/full
- PASADENA Part 1&2 results journal article:
  https://www.nejm.org/doi/full/10.1056/NEJMoa2202867

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 at https://forpatients.roche.com/ and fill out the contact form
- 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 co-organised and co-paid for by F. Hoffmann-La Roche Ltd (headquarters in Basel, Switzerland) and Prothena Biosciences Ltd (headquarters in Dublin, Ireland).

Full title of the study and other identifying information

The full title of this study is: “A Study to Evaluate the Efficacy of Prasinezumab (RO7046015/PRX002) in Participants With Early Parkinson's Disease (PASADENA)”

The study is known as ‘PASADENA’.

- The protocol number for this study is: BP39529.
- The ClinicalTrials.gov identifier for this study is: NCT03100149.

- The EudraCT number for this study is: 2017-000087-15.

Glossary

- **Adverse event** = A physical or psychological problem experienced when taking a medicine
- **BMI** = body mass index
- **Bradykinesia** = slow movements
- **COMT** = catechol-O-methyltransferase
- **DaT-SPECT** = a scan used to confirm the diagnosis of PD by showing how dopamine is working in the brain
- **Delayed-start** = participants in Part 2 who were taking placebo in Part 1 and started taking prasinezumab at the beginning of Part 2
- **Dopamine** = a chemical in the brain used to send messages between nerve cells
- **Early-start** = participants in Part 2 of the study who took
- **Freezing episodes** = where someone is temporarily unable to move
- **Intravenous** = into a vein
- **MDS-UPRS** = Movement Disorder Society-Unified Parkinson's Disease Rating Scale https://www.movementdisorders.org/MDS/MDS-Rating-Scales/MDS-Unified-Parkinsons-Disease-Rating-Scale-MDS-UPDRS.htm
- **MMSE** = Mini Mental State Examination http://www.oxfordmedicaleducation.com/geriatrics/mini-mental-state-examination-mmse/

  The MMSE is a widely used test of brain function: it assesses orientation, attention, memory, language and spatial awareness
- **PD** = Parkinson's disease
- **Placebo** = a 'placebo' looks the same as a medicine but does not contain any real medicine
- **Randomised** = decided by chance which participants will receive placebo or study medicine
- **Resting tremor** = shaking that happens when your body is still and relaxed
- **Rigidity** = muscle stiffness
- **Statistical significance** = calculation used to show if a difference in results is real or due to chance
- **Treatment-related adverse event** = When a physical or psychological problem experienced in a study is due to the study medicine

prasinezumab from the start of the study	