Trial Participation FAQs

1. What is the difference between Analysis Stage 1 and Analysis Stage 2?

Analysis Stage 1 is the first part of the trial. It has recruited 375 participants (in total). Stage 1 participants have up to 4 MRI scans during the first 2 years. Once all Stage 1 participants have completed at least 18 months of follow-up and their MRI scans have been analysed, there is a decision point (this will be approximately in October 2026). The data from these MRI scans along with other data collected, will be analysed to check if the treatments are showing benefit to the participants and if they are safe. At this decision point, if the MRI analysis suggests:

- That a treatment shows sufficient promise of benefit by slowing down changes to the brain in people with MS, then participants taking that treatment and those taking the placebo treatment will continue in the trial.
- That a treatment does not show sufficient promise of benefit for people with ms, participants taking that treatment will stop taking it and their current participation in the trial will be stopped.

Those participants who stop treatment can be re-screened after at least 6 months. If they are eligible, they could be re-randomised to any arms that have continued or to new arms that have been added to the trial.

Analysis Stage 2 is the second part of the trial. It will recruit up to 600 participants per arm (currently maximum of 1800 in total). Recruitment into Stage 2 of the trial will happen in two ways.

- Firstly, people from Stage 1 will move to Stage 2 seamlessly. They will remain in Stage 2 unless their treatment does not show benefit for people with MS (which will be decided using MRI data in approximately October 2026).
- Secondly, new participants screened from 27th November 2024 onwards will go straight into Stage 2. These participants will receive the same treatments as people who entered in Stage 1. They will also follow the same visit schedule and have the same assessments; however, they will not have any MRI scans.

All data collected in Stage 2 will help us understand the safety of the treatments tested in the trial and the potential benefit they could have on MS symptoms and disability.

2. Is Stage 2 the same as the different phases of clinical trials?

No. But there are similarities. Overall, this is a phase 3 trial. This is because positive results would likely lead to treatments being made available for patients in clinical practice.

The stages of the trial refer to what happens to participants and data as the trial progresses. All the stages are equally important, and the treatments and their dosage are the same in Stage 1 and Stage 2

3. When will the MS community know whether current treatments are continuing in the trial?

It is estimated that this decision will be announced in approximately October 2026 based on the data available.

4. How will participants' data be used in the trial if they enter at Stage 1 versus Stage 2?

Data from participants in Stage 1 will contribute to assessing whether the trial treatments appear to be effective and are worth studying further. This is measured by looking at changes in the brain using MRI. If a treatment slows down changes to the brain, this suggests it could also slow down disability progression. Data from all participants (Stage 1 and Stage 2) will contribute to assessing the trial medications safety and whether they have any effect on MS symptoms and disability.

5. How many people will be recruited during Stage 2?

In Stage 2, we plan to recruit 475 new participants per treatment which we expect will continue until at least 2027. These participants will join the 125 participants already on each treatment from Stage 1 who will seamlessly transition into Stage 2. That means the total number of people on each treatment would be 600.

6. How long will Stage 2 recruitment take?

We expect to complete Stage 2 recruitment by end of 2027 approximately.

7. Would it be better to wait to see whether the trial treatments show benefit on MRI scans before joining the trial?

This is up to each individual, but we would advise taking the following into account before making a decision:

Many people who join clinical trials report benefiting from more regular contact with people working in MS (e.g. doctors, nurses, researchers).

- Everyone's data will contribute to research and knowledge, building on what we know about MS, which could benefit people in the future.
- Waiting for preliminary results of a clinical trial before signing up would delay an individual's entry into the trial. Although we hope that the treatments that show benefit on MRI will be effective, this can't be guaranteed.
- If a participant is on an arm that does not continue, they will have the opportunity after at least six months to be rescreened and if eligible to join the trial again if they wish.

8. When might new treatments be added to the trial?

We are constantly screening potential medications for their promise in treating MS. The earliest new treatments would be added to the trial is 2026.

9. What happens if a participant joins an arm that is continuing at the decision point?

If their treatment continues in the trial, then they will continue to take that treatment and have regular trial visits for up to 5 years.

10. What happens if participant joins an arm that is dropped? How soon can they re-enter the trial?

Analysis of MRI data from Stage 1 may indicate that a treatment does not appear to have benefit for people with MS. This treatment will then be stopped. If this happens, participants who are on that treatment will have a final visit with their trial doctor, who will arrange for them to revert to their normal clinical care. If these participants would like they may be offered the opportunity to join the trial again after at least 6 months if they are still suitable for the trial.

11. What happens to participants who joined Analysis Stage 1 and what happens to their data?

Participants who joined in Analysis Stage 1 will continue as before in the trial. This includes taking the trial treatment, attending the trial visits and having their MRI scans

The data from all trial visits will be used to decide which treatments should continue in. In approximately October 2026, the trial team be able to confirm whether the treatment they are receiving will be continuing in the trial or not. If the treatment is continuing, then nothing will change and their data from all the trial visits will be used to assess whether that treatment is safe and has an effect on MS symptoms and disability.

However, if the treatment is being withdrawn then those participants will be contacted to attend an end of trial visit and discuss next steps.