

Dear xxxxx

We are writing to update you with important information about the DiPALS study in which you are a participant.

At the last safety meeting the results indicated that pacing was of no benefit to patients with ALS and may in fact be causing harm. **We are therefore asking all patients in the study to stop using their pacing systems immediately.**

- Your local study team will talk to you about how to do this.
- We do not anticipate stopping pacing will lead to any problems for you.
- If you do experience any worsening of symptoms or new symptoms on stopping pacing then please let you study team know.
- The contact details of your study team are xxxxxxxxxxxxxxxxx

It is important that you continue to use Non Invasive Ventilation (NIV). This is a safe and effective treatment for breathing problems in ALS patients.

Once you have stopped pacing your study team will organize collection/return of your pacing box. The pacing wires that are attached to you can be dealt with in one of three ways:

1. Left as they are. There is no evidence to suggest the presence of the wires is harmful. It is safe to leave them as they are.
2. The wires can be cut as they leave the skin. You would have no wire visible but the inside part of the wires would be left in.
3. You can be given a local anesthetic in the skin where the wires are located and the wires can be pulled out.

Although we have asked participants to stop pacing it is very important to continue to monitor individuals for safety reasons and to gain as full a picture as possible regarding the effects of pacing in patients with ALS. We therefore ask you to continue with your study visits until your 12 month visit or the planned end of the study.

The full study results are not yet available and will not be available until the end of the year or early next year. However, it is clear that pacing adds no benefit to the group of ALS patients included in the study. We will hopefully have more of an understanding when we have had the opportunity to analyse the full study results.

We understand that this news will lead to worries and many questions. Your study team are available to answer your questions in detail. We have compiled a list of questions and answers to give you some more information, enclosed with this letter.

We would like to take this opportunity to thank you for your contribution to DiPALS. We realize that taking part in clinical studies is itself a burden on individuals and those who support them. DiPALS is an important study and when the full results are available will help doctors and individuals with ALS to be able to make informed decisions about the best treatments for ALS.

Yours sincerely,

Local PI team

Further Questions and answers

Why do I have to stop using my pacing device?

The DiPALS study has a Data Monitoring and Ethics Committee (DMEC). The primary role of the DMEC is to monitor safety of participants taking part in DiPALS. They have analysed the data from the study and have identified that pacing is of no benefit to patients with ALS and may in fact cause harm.

What harm has pacing done to me?

The results suggest that patients who received pacing in addition to Non-Invasive Ventilation did not live as long as patients receiving treatment with NIV alone. The size of the difference in survival will be calculated once we have completed the study. On the data available so far survival is certainly no better in patients receiving pacing and may be worse.

What happens if I feel worse on stopping pacing?

We do not expect this to happen. However if you experience problems on stopping pacing please contact your study doctor. It may be that using your NIV more may help.

I feel pacing helps me and I would like to continue to use it?

The instruction from DiPALS is that all patients stop pacing. Any contrary decision to continue pacing will be taken by your consultant, yourself and local hospital outside of the DiPALS study. The responsibility for continuing pacing will rest with your consultant.

What do I do with the wires attached inside of me now that I have stopped pacing?

The pacing wires that are attached to you can be dealt with in 1 of three ways:

1. Left as they are. There is no evidence to suggest the presence of the wires is harmful. It is safe to leave them as they are.
2. The wires can be cut as they leave the skin. You would have no wire visible but the inside part of the wires would be left in.
3. You can be given a local anesthetic in the skin where the wires are located and the wires can be pulled out.

I have been given NIV as part of the trial. Is that safe?

Yes. NIV is a safe and effective treatment for breathing problems in ALS. You should continue to use NIV as much as possible.