EXPERTS-ALS: Website Summary - Metformin and Nifedipine Interim Analysis Results

Headline result:
The EXPERTS-ALS study has found that **Metformin and Nifedipine do not lower neurofilament light chain levels** in the blood. As a result, we will now stop entering new participants onto the Metformin and Nifedipine arm of the study.

We explain what this means for the trial and the wider MND/ALS community below.

What is EXPERTS-ALS?
EXPERTS-ALS is a research study designed to **screen drugs rapidly** for their potential to slow the progression of MND/ALS. We do this by looking at changes in a blood test marker called neurofilament light chain.

- **Lower** neurofilament levels are linked to a **slower rate of disability progression** in people with MND/ALS.

EXPERTS-ALS is not designed to prove whether a drug provides clinical benefit to people living with MND/ALS, defined as how someone feels, functions or survives. It can only look for an early signal of disease-slowing. It aims to quickly identify the most promising drugs to go forward into the larger clinical trials needed to test this (phase 3 trials). When we do identify a drug which results in a large and important reduction in neurofilament levels and potentially slowing MND/ALS progression, we will recommend that it is prioritised for clinical benefit testing in a phase 3 trial.

What is an interim analysis?
An interim analysis is when the results are reviewed during the study whilst participants are still taking the study drugs.

When an interim analysis shows that a drug does not appear to be statistically lowering neurofilament levels, we stop testing it in new participants. It does not mean that the stopped drugs have caused any harm. These decisions follow strict guidelines agreed upon by a group of expert doctors and researchers before the study started.

What were the results for Metformin and Nifedipine?
An independent group of doctors and statisticians has reviewed the data collected so far.

The results showed that the **neurofilament level for Metformin and Nifedipine has not changed**. This means that the drug does not meaningfully slow down the disease process in MND/ALS. The independent oversight group recommended that we **stop testing this drug in new participants**.

Who was included in the analysis?
Metformin:

- 36 participants were treated with Metformin.
- 22 participants provided the blood samples at week 18 used for the analysis.
- 5 participants stopped treatment prior to week 18. Their data remain an important part of the study's overall dataset.

Nifedipine:

- 31 participants were treated with Nifedipine.
- 18 participants provided the blood samples at week 18 used for the analysis.
- 1 participant stopped treatment prior to week 18. Their data remain an important part of the study's overall dataset.

What does this mean for individuals?

Participants who are currently taking Metformin and Nifedipine will stop taking the drug, either immediately or at their next study visit. This allows us to gather all of the data and check for the possibility that some participant neurofilament levels have responded differently to others. It is important to say that the stopping of a drug arm in this type of analysis is **not** because of safety issues. There is no evidence that either drug has caused harm.

The results do not affect the treatment of participants currently taking one of the other study drugs.

What does this mean for the study?

We understand that it may be disappointing to hear that Metformin and Nifedipine do not lower neurofilament levels. However, this is an important milestone for EXPERTS-ALS and the data collected from the participants are still extremely useful to advance knowledge. It also shows that the study design is working as intended, allowing us to quickly decide which drugs are unlikely to lower neurofilament levels.

"The quick rejection of [arm] is what our community needs. Yes we would have rather seen a quick identification of a positive hint, but not spending 3 years, with placebo, is exactly what research needs. Screen, discard and move on. Speed" – Lee Millard, EXPERTS-ALS PPIE Representative

"It's disappointing, of course, that this/these candidates are not suitable to go through to a Phase 3 trial, but it is great to see the "proof of concept" emerging. Experts-ALS is designed to considerably shorten the overall length of the trial process so that only the most likely drugs go through to the next phase, meaning considerable savings in terms of time, but also funds wasted on candidates, which are unlikely to work or only have very marginal benefit. I'm excited to hear that novel drugs are going to be tested as well as repurposed ones." David Setters, EXPERTS-ALS PPIE Representative

What happens next?

We will write up the full results to publish them in a medical journal and share a summary on our website.

We have an expert panel of doctors and scientists identifying new drugs to be included in the study. In future, this is likely to include novel compounds as well as repurposed drugs (drugs which are already used to treat other conditions). In the meantime, EXPERTS-ALS remains open and active. We are continuing to recruit new participants for our other drug arms: Ropinirole, Doxycycline and Salbutamol.

Thank you

We are grateful to all of the participants who have generously given their time to take part in this study. We cannot advance the road to effective treatment without them and thank them on behalf of all those living with MND/ALS.