Frequently Asked Questions related to the Clinical Development of Arimoclomol in ALS during the COVID-19 Pandemic

Will the ALS trials with arimoclomol continue?

The ORARIALS-01 double blind phase 3 trial will continue with some changes applied to make the evaluation of the trial participants possible from a practical perspective.

The ORARIALS-02 trial has safety monitoring similar to the ORARIALS-01 trial however there is a requirement for more frequent safety monitoring in the first 6 months as this will be the first exposure to arimoclomol for 33% of the participants. The trial continues at this time, however the evaluation of how to handle the more frequent visit schedule (blood sampling) continues to be investigated.

Is there any additional risk in taking Arimoclomol?

Arimoclomol is a small molecule that amplifies the expression of heat shock proteins (HSPs), in particular Heat shock protein 70 (HSP70), in cells under stress. HSPs are part of a natural cellular defense system with neuroprotective properties that prevent aberrant misfolding and aggregation of proteins. There is no evidence to suggest that administration of arimoclomol alters the risks associated with COVID-19.

Does Trial participation place the participant and their family at increased risk?

Older adults and people of any age who have serious underlying medical conditions may be at higher risk for more serious complications from COVID-19. (WHO: https://www.who.int/health-topics/coronavirus#tab=tab_1)

The mean age of onset of ALS is between 55 and 65 years. People with ALS will experience difficulty breathing making them a vulnerable population.

The trial 'per se' poses no new identified risk to the participants as a result of the COVID-19 outbreak. However, conventional clinical trials require participants to attend public spaces and interact closely with those providing their care. This not compatible with themes such as 'self-isolation' or 'shielding' and as such the protocol will have an addendum served for the period of the COVID-19 pandemic to ensure that risks to participants are minimized.

What actions are being taken to reduce the risks to trial participants?

Our trials have been designed in such a way that participation should add as little additional burden as possible, while conforming to disease specific guidance on clinical trials. As such, we do have some patient-first features already being utilized.
Below we describe these features, which are now being upscaled or newly implemented as a result of COVID-19. The described services may require IEC/IRB or institutional approval and hence may be restricted to only some trial sites or geographies.

A) Participant Travel Reimbursement

We continue to reimburse participant travel expenses as per the limits applied by IEC/IRB (as appropriate). We will however promote the use of services which limit social-interactions or avoid public spaces such as taxi services.

A debit card program is already in place and so the subjects should not experience any additional concerns regarding the ongoing cost of trial participation since out of pocket expenses are covered. The exact nature of how the value is transferred to the participant and their caregiver is site specific.

B) Remote Visits / Telemedicine

Where attendance to the clinical site is not possible, advised or favored by the participant, we support the use of a telephone observation visit. The primary efficacy measure ALSFRS-R will continue to be possible and is validated for use via telephone.

C) Home Nursing Services

We already have a home nursing service in place, and we will expand the use of this to all participants as required, whereas this service was previously restricted to home-bound participants only.

D) Study Drug Supply

A specific service which allows study drug to be shipped directly from the pharmacy to the participant's home/residency is in use. This service has all required approvals in place and special precautions are taken to protect personal information.

Trial participants may be provided with additional study drug supply to prevent any restrictions on their access to study drug as a result of hospital pharmacy closures etc. This will only take place where it is safe to do so.

The vast majority of subjects will receive study drug to last them until the end of the trial. For those participants that have not progressed so far through the trial to date, an additional 4 months will be supplied on top of the usual dispensing schedule. Arimoclomol (and placebo) are very stable products and may be stored in the participants home providing a small number of measures are taken as described in the Patient Information Leaflet.

E) Clinical Safety Laboratory Testing

We are working to supplement the site staff telephone by a visit to the participant's home/residency to allow for a clinical safety laboratory test. If this is not possible, the participant may use a local laboratory in lieu of the trial central laboratory during the time of the COVID-19 pandemic. We may be required to instruct the participant to pause using the study drug if clinical safety laboratory testing is not available.

Will the trial design change?

The clinical trial protocols will have an 'addendum' applied which is intended to be in place for as long as needed due to COVID-19 restrictions. Once the national restrictions are lifted, the original protocol will preside.

It may no longer be advisable to measure some of the trial endpoints such as SVC.

Orphazyme is continually reviewing the national / regional limitations and the evolving regulatory guidance to ensure that the trials can be conducted in a compliant, safe and practical manner.

How will the changes be communicated to trial participants?

The Principal Investigators (PI) and their trial teams will be informed of the changes to trial conduct through the issuance of a protocol addendum that will be disseminated to PIs and implemented in a timely manner.

The changes to the planned trial activities will be communicated to the participant by the site staff and they will also be required to document evidence of consent to the changes.

We would strongly encourage that any questions received by the patient advocacy community are shared with Orphazyme and that the trial participants are encouraged to maintain their dialogue with the trial team to ensure that they have the most up-to-date information regarding the specific restrictions applied at that research site.

How does COVID-19 affect Orphazyme's ability to support the community?

Orphazyme R&D staff are located in Copenhagen, Denmark. As of 16th March 2020, Denmark's national restrictions apply with the consequence that our team are working remotely. We apologize for any inconvenience that this may cause, as a result of greater demands for coordination and communication. Additionally, Denmark's Boarders are closed and so the team are not able to travel at this time.