FALCON

Inclusion Criteria

- Age 18 years or older.
- A confirmed PMD diagnosis caused by a known pathogenic gene mutation or deletion of the mitochondrial genome (category 6 of the International Classification of Inborn Metabolic Disorders [ICIMD])12 according to American College of Medical Genetics (ACMG)/Association of Molecular Pathology (AMP) criteria1, with multisystemic disease expressions, including:
- m.3243A>G associated MELAS-MIDD spectrum disorders,
- single large scale mtDNA deletion associated KSS-CPEO spectrum disorders,
- other multisystemic mtDNA-related disease (including MERRF).
- Presence of chronic mitochondrial fatigue:
- History of mitochondrial fatigue for at least 3 months prior to the Screening Visit AND
- Presence of at least moderate level of fatigue, assessed by PROMIS® Fatigue PMD Short form raw score ≥ 27 at Screening and Baseline
- Presence of mitochondrial myopathy defined as:
- Myopathy (proximal muscle weakness), NMDAS Section III Clinical Assessment, item 5 score ≥ 1, which reads: ”mild but clear proximal weakness in hip flexion and shoulder abduction - MRC 4/5”. For the inclusion only hip flexion, but not shoulder abduction, should be taken into account. AND / OR
- Exercise Tolerance: NMDAS Section I, item 9 score ≥ 1, which reads: ”unlimited on flat - symptomatic on inclines or stairs”.
- Patients must be able to perform at least 2 repetitions and the maximal capacity must not exceed 17 repetitions in males or 16 repetitions in females in a 30s STS test at screening.
- Clinically stable, apart from symptoms associated with the diagnosis of mitochondrial disease, at Screening and Baseline, as determined by medical history, physical examination, 12-lead ECG, vital signs measurements, and clinical laboratory evaluations at Screening, as assessed by the investigator.
- The patient is willing and able to attend study appointments within the specified time windows.
- Willingness and ability to complete electronic PROs.
- Willingness to maintain a stable diet during the Screening and study periods.
- Patients who take any mitochondrial disease-focused vitamins or supplemental therapies, including coenzyme Q10 (CoQ10), has been on a stable dose regimen of these for 3 months prior to randomisation and intends to stay on a stable dose for the duration of the study period.
- Willingness to suspend treatment with idebenone during the study.
- Female patient is not pregnant and at least one of the following conditions apply:
- Not a woman of childbearing potential (WOCBP)
- WOCBP must agree not to try and become pregnant and use a highly effective method of contraception from the time of informed consent through at least 36 days (~5 half-lives of KL1333 plus 30 days) after the last dose of investigational medicinal product (IMP) administration.
- Male patients with female partner(s) of childbearing potential must agree to use a male condom in addition to using highly effective contraception throughout the treatment period and for 96 days after the last dose of IMP administration. The requirement to use a male condom also applies to male patients with a pregnant or breastfeeding partner.
- Female patients must agree not to breastfeed starting at Screening and throughout the study period and for 36 days after the last dose of IMP administration.