Understanding the FALCON Study, investigating a potential therapy for mitochondrial disease

Mary Kay Koenig, MD
UTHealth Houston
Center for the treatment of Pediatric Neurologic & Neurodegenerative Disease
Mitochondrial Center of Excellence

Fatigue

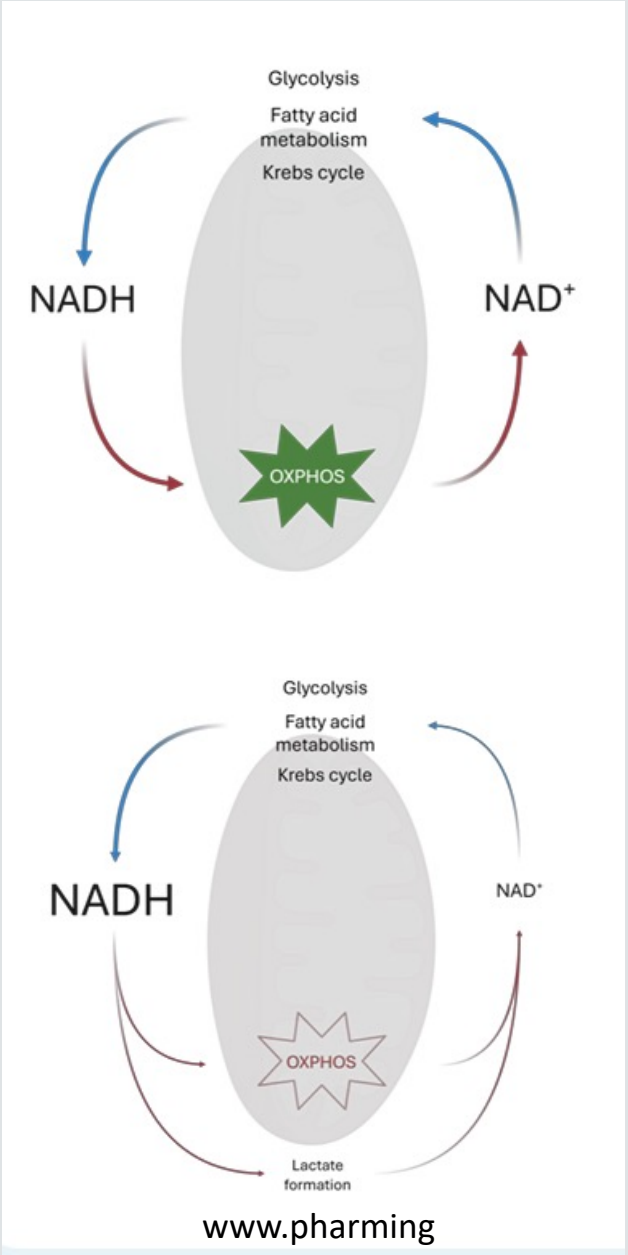
- Fatigue is defined as an extreme or persistent tiredness, weariness, or lack of energy that does not go away with normal rest
- Signs of fatigue:
  - Low energy – constant exhaustion that does not go away with sleep
  - Muscle weakness – muscles feel heavy, weak, or sore without doing hard work
  - Slow reactions – slow reflexes and poor hand-to-eye coordination
  - Brain fog – trouble paying attention, remembers things, or even making simple decisions
  - Mood changes – feeling easily annoyed, sad, or unmotivated

Mitochondrial Fatigue

- Fatigue is a primary and debilitating symptoms of mitochondrial disease for many patients with >70% reporting fatigue in some studies
- The etiology of fatigue in mitochondrial patients is likely multi-factorial with depression, anxiety, and sleep disturbance contributing
- Mitochondrial disease also leads to both a lack of energy production within cells, energy required for muscles to function, and a buildup of toxic waste products, such as lactic acid, that can lead to fatigue and exhaustion

NAD+/NADH Ratio

- Normal cellular energy production is partially regulated by the balance of NAD+ and NADH within cells, ie, the NAD+/NADH ratio
- In mitochondrial disease, the NAD+/NADH ratio is altered leading to reduced energy production



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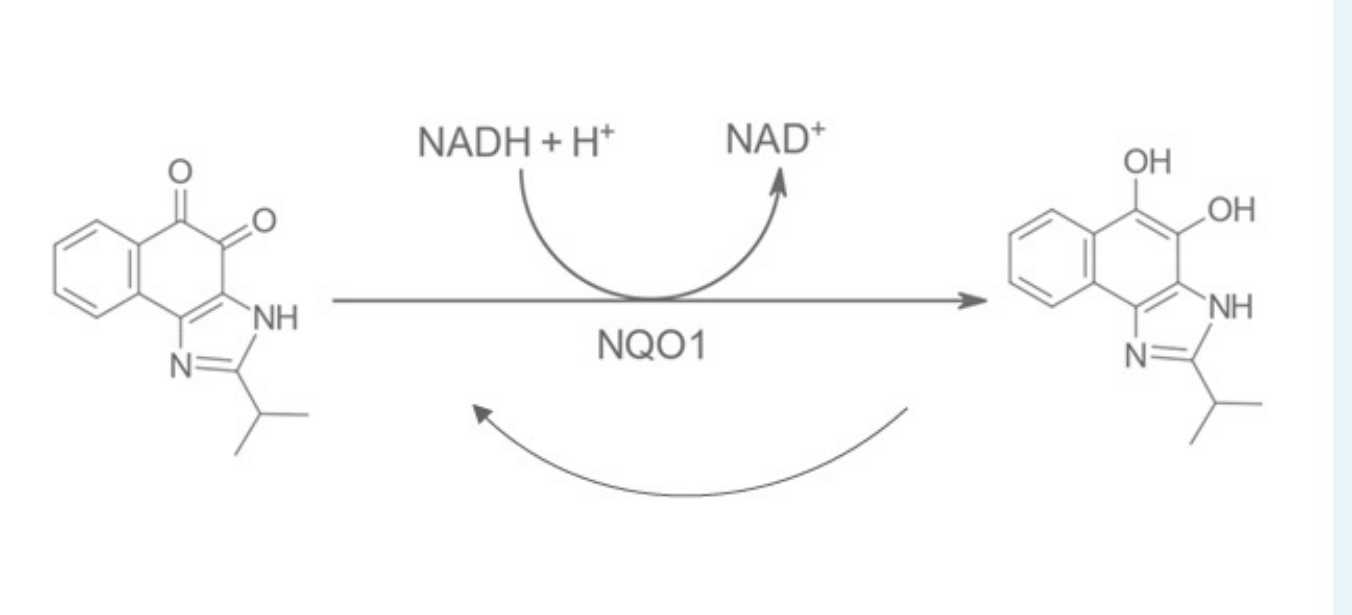
Napazimone (KL1333)

- Napazimone is an investigational drug designed to restore the NAD+/NADH ratio within the mitochondria thus stimulating ATP synthesis



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FALCON STUDY

- In the FALCON study, researchers want to know:
  - Does the study drug, napazimone (KL1333) improve symptoms of fatigue in patients with mitochondrial disease?
  - Does the study drug improve physical abilities?
  - Does the study drug improve a person's ability to carry out their daily activities?

FALCON Study Assessments

- Subjects will answer questionnaires to help assess if the study treatment is working
- Assessed at in person and/or home visits:
  - **PROMIS sleep disturbance scale** – subjects are asked to rate their sleep within the past 7 days by answering 4 questions using a 5 point scale
  - **Individual Activity Assessment** – subjects identify 3 activities that are performed on a regular basis (hobbies, chores, work tasks, etc.) and rates them on how much their mitochondrial disease interferes with their ability to perform the activity over the last 7 days on a scale of 1 to 5 (mild interference to unable to perform the activity)

FALCON Study Assessments, Continued

- **Patient Global Impression** – patients will rate their overall impression of severity and change in severity of fatigue and lower extremity function over the last 7 days
- **Neuro-QOL Extremity Function** – subjects are asked to rate their ability to carry out various activities involving their legs and trunk
- **Pain scale** – subjects will rate their pain experience and intensity from “0” representing no pain to “10” representing extreme pain over the last 7 days
- **5-level EuroQol-5 Dimension** – this scale assess mobility, self-care, usual activities, pain, and anxiety/depression. It is used as an assessment of “overall health” 30 second sit-to-stand – measurement of lower extremity strength and endurance

FALCON Study Assessments, Continued

- Performed weekly at home:
  - **PROMIS fatigue PMD** – 9 questions answered “never, rarely, sometimes, often, or always” designed to measure the concept of fatigue specifically in patients with mitochondrial disease
  - **Insulin use diary** – for those patients taking insulin
- Study physicians will also perform a clinician global impression scale and another mitochondrial disease assessment at study visits to assess overall disease progression/improvement during the study

FALCON Study

- Who might be eligible to participate in the FALCON Study?
  - You must be at least 18 years old
  - You must have a mutation or deletion in the mitochondrial DNA (mtDNA)
  - You must have chronic fatigue and myopathy, ie, muscle weakness or exercise intolerance

*other study inclusion criteria will be reviewed individually with the study team if those interested in participating

FALCON Study

- What to expect if you participate:
  - 5 to 8 study visits (3 may be done at home)
  - Monthly telephone check-ins with the study team
  - Oral study treatment is taken twice a day
- What not to expect:
  - Expenses – all study related costs are covered and there should be no cost to you to participate
  - Changes to your supplements – you may continue to take all of your supplements as long as you don't change them while participating
  - Long travel – there are lots of study sites around the country so there should be one close to you

FALCON Study Timeline (61-65 weeks, 15-16 months)

Screening	Treatment	Follow-up
• Testing to see if you meet the criteria to participate in the study • 1-2 clinic visits 8-12 weeks	• Receiving the study drug • 2-3 clinic visits • 3 at home nurse visits • Monthly phone visits 48 weeks	• 1 clinic visit • Optional continuation in 48 week extension study 5 weeks

FALCON Study Randomization

- For every 5 study participants, 3 will receive napazimone (KL1333) and 2 will receive placebo
- Neither participants nor the study team will know which subjects are receiving the study drug and which are receiving the placebo
- This lets researchers compare the results fairly

Napazimone (KL1333) known side effects

- Napazimone has been studies in some healthy people and in people with mitochondrial disease previously
- The risks and effectiveness are not fully known, but some side effects reported in people taking it previously include:
  - Abdominal discomfort and pain
  - Diarrhea
  - Bloating
  - Nausea
- If you experience any of these, or other, symptoms while on the FALCON study, please report them immediately to your study team

Why should I join the FALCON Study?

- Joining a clinical trial is an important and very personal decision. It should be discussed with your friends, families, trusted confidants, and physicians before making any decisions.
- Joining any clinical study helps researchers understand if the study drug works as it is intended to improve symptoms of the disease under study.
- ***Joining the FALCON study will help investigators learn if napazimone works to improve the symptoms of mitochondrial disease in patients and may advance therapy for everyone.***

For more information on the FALCON Study

- FALCON Study information: www.falconmitostudy.com
- FALCON Study site locations: clinicaltrials.gov/study/NCT05650229
- Clinical Trials information: www.mitoaction.org/clinicaltrials

Thank you!

UTHealth Houston

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