Why is the EDELIFE Clinical Trial, studying a potential treatment for XLHED, only for boys?

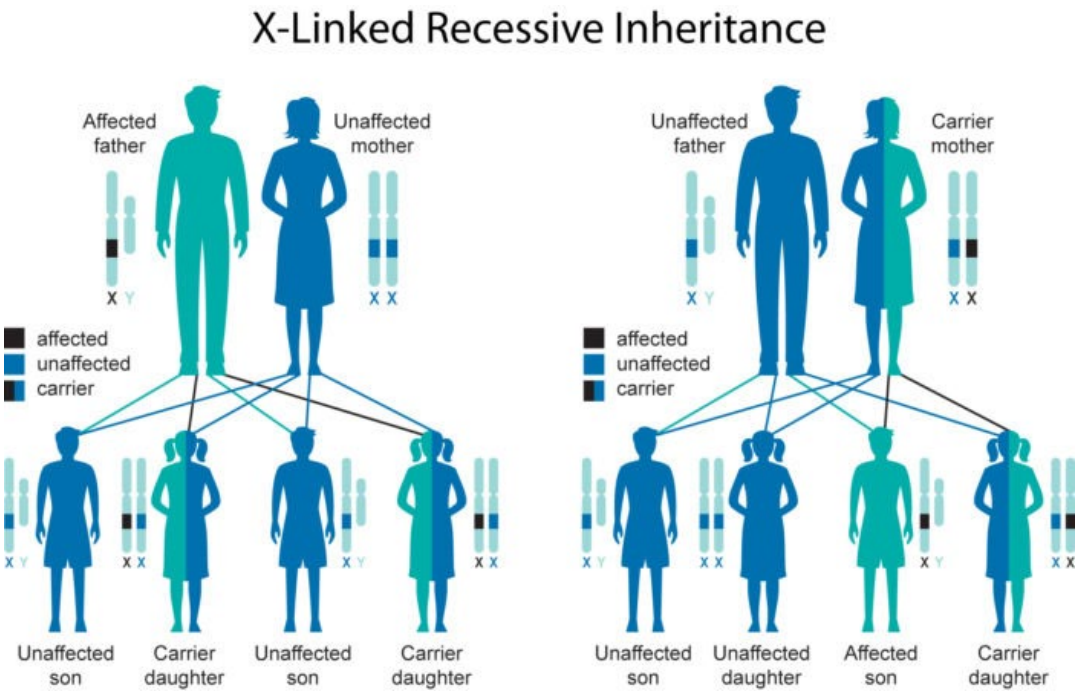
The answer is directly related to how x-linked hypohidrotic ectodermal dysplasia (XLHED) is inherited, or passed down from parents to children, and the best practices for studying potential drugs. This includes having consistent baselines to measure symptom reduction and ensuring the benefit of the treatment outweighs any potential risk to the participant. Once the treatment is approved for use in boys, it will be considered for use in girls as well. Learn more, here.

1. Genetics

The gene responsible for X-linked hypohidrotic ectodermal dysplasia (XLHED) is the ectodysplasin (EDA) gene, which is located on the X chromosome. The EDA gene is responsible for the production of the protein ectodysplasin A1 (EDA1), which signals the development of ectodermal structures (such as hair, teeth, skin, sweat glands, etc.). In XLHED, the EDA gene is faulty and does not produce working EDA1, leading the symptoms of XLHED.

Boys only have 1 X chromosome, and if they inherit the faulty one from their mothers, they will not be able to make any EDA1 and will be fully affected by XLHED, showing the full range of symptoms.

Girls on the other hand, have 2 X chromosomes, and if they inherit a faulty one, the issues they would experience can be partially compensated by the other fully functioning X chromosome.



This is why XLHED symptoms in girls vary and may be mild to non-existent and is why boys with XLHED are always affected and consistently more so than girls.

2. Benefit/Risk Concept in Drug Approval

Drugs can provide a significant relief, but they also carry risks. For a new drug to be approved by the health authorities, such as the FDA, the criteria is always what is known as the "risk/benefit balance." In short, this means that a drug must demonstrate that it provides a substantial benefit, such that it outweighs the risks of giving it.

Boys with XLHED are consistently severely affected. They represent a homogenous population, or group where the individuals have the same genetic makeup and symptoms. Therefore, the consistent expression of symptom boys means we can demonstrate if a response is directly linked to the drug. In girls, there is variability of the observed XLHED symptoms. If a girl showed mild or no symptoms, it would be difficult to determine if that was due to the drug or if they would have had those same symptoms without the drug. Conversely, as the boys are consistently more severely affected, the potential risks associated with administering the drug are also more justifiable in boys.

So demonstration of "benefit" linked to the drug is more likely to be achievable in boys. And demonstration that the "benefits" outweighs the risks is also more likely to be achieved in boys.

The Edelife clinical study is therefore only for boys because of the consistent and more severe symptoms experienced in males with XLHED. This consistent starting point will allow any recovery of ectodermal structures and improvement of XLHED symptoms to be attributed to the drug, ER004, which is a synthetic version of the EDA1 protein. This is the most rapid and most likely path to obtaining an approved drug for XLHED.

Once ER004 is approved for use in boys, we will consider administering ER004 to girls.