SPEAKER: Inpatients with zero enzyme activity and a nonsense mutation or a frameshift mutation, in the United States, there's really only one option for therapy at this time. And that's enzyme replacement therapy, which is an IV infusion of alpha-galactosidase A. And that works by replacing the enzyme that's missing.

If you have a patient with a mutation that has some potential residual activity, the patients may be candidates for a chaperone therapy. The way the chaperone works is by binding to the enzyme and maintaining a stable conformation of the enzyme during transport to the lysosome. And then the chaperone drug releases the enzyme, and the enzyme is able to do its job.

Not all mutations with residual enzyme activity are responsive to the chaperone, so you really need to check on the chaperone therapy to make sure that the specific mutation that you have identified is, in fact, amenable or responsive to that drug. If it is, it stabilizes delivery of the enzyme into the lysosome, and then when the chaperone drug detaches from the enzyme, the enzyme becomes potentially active and can do its job.

Now, there is variability on the amount of response, but we have some mutations that will go from a measured activity as low as 0.4% or 0.5% of expected up into the range of 30% or higher, which is an excellent response. And those patients would be good candidates for the chaperone therapy.

Some mutations, however, just don't respond to the chaperone therapy. And for those patients, only the ERT would be. Now, ERT can be used in any patient with a diagnosis of Fabry disease because they you're putting an exogenous enzyme. And it should be taken up by the cells in the body.

There are some differences in the way in-- who would be good candidates for the various therapies. So for example, patients who are having difficulty tolerating the enzyme therapy, either because of infusion-related reactions or just because they don't like the IV and the amount of time that's required for enzyme infusions, if they have an amendable mutation would be potential candidates for the chaperone therapy. Patients who are not tolerating the chaperone therapy, for example, because of headaches may wish to switch from the chaperone to the enzyme therapy. So there are potentially multiple different approaches to the treatment options.