

Risk vs. reward



Jim Williams

As researchers learn more about muscular dystrophy and its genetic make-up, clinicians all over the world are readying drugs and therapies that they think will help those with MD. Many families are willing to risk everything for the hope of a cure.

Families whose children have a diagnosed disease covered by the Muscular Dystrophy Association are sometimes identified by their treating physician to be candidates for clinical trials to determine the effectiveness of these treatments on human beings.

There is risk and potential reward for those who participate. The process of bringing a drug or therapy to human trials is long and slow for a

purpose. The history of our country has shown that without proper testing, drugs can have a destructive impact. Balancing the hope of a therapy is the risk and reward that exists in this process. No company should be allowed to gain profit unless an informed person can make a rational decision about the trial.

Twenty-year-old Carlie Brinker of Millersburg, OH, knows what it's like to have a chronic, disabling condition and to have to take medications that come with many side effects.

When she was 8 years old, she learned she had dermatomyositis, an inflammatory muscle disease involving weakness, pain, rashes and calcium deposits under the skin that can lead to serious infections.

Over the years, she's taken anti-inflammatory corticosteroid drugs; methotrexate, an immune-system suppressant; intravenous immunoglobulins, which redirect the immune system; and several other medications. All of them have potentially serious side effects. Prednisone had caused significant weight gain, severe mood swings and high blood pressure.

In 2006, at the suggestion of her doctor, she entered a Phase 2 trial of rituximab, a drug used to treat rheumatoid arthritis and lymphoma that blocks B cells, which are part of the immune system.

Brinker learned she would get four intravenous infusions, two of rituximab and two that would be a placebo (inactive, look-alike substance). "They said it might or it might not work for me," she recalls.

She remembers signing papers that warned of the risk of infection and described blood tests and a muscle biopsy. She learned she would have to discontinue her intravenous methylprednisolone, her immunoglobulins, and her colchicine, a drug she was taking in hopes of warding off further

calcium deposits. "I was a little scared about that," she says, recalling that she did develop more calcifications.

Discontinuing the immunoglobulins also worried her. "Since I can usually tell by the third week that it's time to get it, I was scared about that. I was really tired and worn out." Likewise for the I.V. methylprednisolone. "I didn't have a lot of the energy that I had while I was getting it," she says.

Despite these concerns, Brinker decided to enroll in the trial. "At that time, I was willing to try anything," she says. "Not only for me, but for the other kids, to try to give hope to us to find a cure and not have so much pain."

In fact, Brinker says, rituximab didn't help her, but it did help others in the trial. One boy, she says, "was in a wheelchair, and now he can walk. After only two infusions, they were able to lower his prednisone. Although it didn't work for me, I have a couple of friends getting ready to start it, and I'm hoping it works for them."

Anyone who's participated in or conducted a clinical trial in the last several years knows that the enterprise is highly regulated.

There are papers to be signed and filed showing that patients have consented to the trial's procedures and understand the risks; institutional review boards looking over investigators' shoulders to make sure everything is in compliance with regulations; reports to file with the U.S. Food and Drug Administration (FDA); and data and safety monitoring committees standing ready to interrupt a trial if there are signs of danger.

"We were given tons of documents; it was like reading a book," says Hank Santini, 54, of Bolton, MA. Santini, who has the late-onset form of the metabolic muscle disorder Pompe disease, recently participated in a trial of Myozyme, a synthetic enzyme developed by Genzyme Corp. that had been proven effective in infantile-onset Pompe. (The results of this trial ultimately showed Myozyme to be effective in late-onset Pompe disease as well.)

"They told us about all the problems that they had with the children [in the previous trial]," says Santini. Every single mishap was detailed. It was all in black and white: These are things that have happened; these are things that could happen."

Such thoroughness may seem excessive or even obstructive. "Any time anything happened, anywhere at any of the test sites, you were given another set of forms to read," Santini recalls.

The FDA, which gets a great deal of criticism from those who want treatments to be approved more quickly, is a safeguard against unscrupulous people who would attempt to use a patient's fear against them. MDA works closely with the FDA to properly test these treatments.

All of us would like to see worthwhile therapies approved sooner. After all, MDA is in the business of providing help and hope. Our hope is that one day, a treatment and cure will be provided that is safe and well tested.