IBM Follistatin trial: one man's report

Shortly before TMA's Annual Patient Conference, TMA Board of Directors Chair Augie DeAugustinis let colleagues know they might be surprised at first when they saw him in Reno. "You'll notice I'm walking a lot better and have better balance," he said. This was wonderful news for Augie and for everyone with inclusion-body myositis.

Augie is participating in the Follistatin Gene Therapy Clinical Trial led by Dr. Jerry Mendell at Nationwide Children's Hospital in Columbus, Ohio. He had been selected to be one of the three to receive high-dose injections in both legs. Augie was injected in January, 2014.

Augie gives us an inside glimpse of the meticulous preparation for a trial of this magnitude and importance. In his case it included an initial biopsy so there would be a baseline for comparison, then a waiting period of eight weeks so the biopsy site could heal. Before his legs were injected, Augie also had an MRI (magnetic resource imaging) both for comparison purposes and to guide the researchers to the appropriate injection sites. Augie said he'd been told that it's crucial to choose good muscle for these injections.

The injection itself was not painful, he recalls. He checked into a hospital room in the morning, and was examined by Dr. Mendell. The doctor identified three areas on his leg with purple circles, based on the information from the MRI and ultrasounds. Augie received a mild sedative, then was injected with a small needle, about the size of a needle used for a flu shot.

Augie received 12 injections in each leg, in what doctors marked as the healthiest part of his muscle. Ideally, he said, the injections would be distributed throughout the leg, but some of his muscles, particularly in the middle of his leg, were so atrophied that his injections were more concentrated within the healthiest muscle. "It was completely painless," he said. The procedure took about 45 minutes. To make sure there was no immediate adverse reaction to the study drug, Augie spent the night in the hospital, where staff checked periodically for redness, pain or any other ill effects.

With that behind him, Augie was released to his daily life as a human guinea pig. Two other IBM patients were injected at about the same time with the same level of dosage in both quadriceps.

His first sense of improvement was vague and he wondered if it was subjective: "It seemed like I could walk farther and faster," he said. Starting at about three months, he was comfortable believing this was an accurate observation, and it was confirmed by his timed walk at Nationwide Children's Hospital.

At about the same time, something even more startling happened. Augie had been instructed to carefully preserve the markers that identified the injection sites. This meant that each time they started to fade from wear or washing, he meticulously renewed them with a purple marker.

Augie watched the markers on each leg as they moved farther and farther away from the actual scar. "I was concerned, but also excited," he said. When he checked with the researchers they were excited, too, he remembers: "They said, 'of course! This is what we expect.'" Augie's skin was being stretched by the growth of new muscle. Augie could also see and feel firm new muscle, and — best of all — he could cover significantly more ground in six minutes than he'd been able to at the start of the trial. He also experienced better balance and less fatigue.

What's in Augie's future? The only response is from muscles that were actually injected, so Augie still has weakness in his hands, and he still finds it difficult to go upstairs. Augie was told that his muscles may continue to grow for a year. This doesn't mean that he doesn't have IBM anymore: he was told that the disease will continue to attack his muscle, although possibly at a slower rate. "The follistatin seems not only to build muscles at the injection site, but to dampen the inflammation," he said. And Augie's efforts — and those of the others in the trial — will pave the way for future treatment. "The evidence is overwhelming that this is safe," Augie said. "Future trials may use significantly higher doses and more muscle groups."

See Follistatin, page 17.

BYM338 trial advances

IBM patient Craig Patterson received his fifth infusion of the trial drug BYM338 (also called bimagrumab) at the end of September. Craig suspects that he is receiving the drug rather than the placebo because he has had some mild symptoms that are typical side effects of the drug.

Craig is receiving his infusions at Kansas University Clinical Trial Center. He is walking farther in the timed walk, but is not sure yet if it is a significant change.

Novartis updates information about its trials at the website www.clinicaltrials.gov, but patients have found some information to be contradictory. One trial, "Efficacy and Safety of Bimagrumab/BYM338 at 52 Weeks on Physical Function, Muscle Strength, Mobility in sIBM Patients (RESILIENT)" has 43 sites throughout the world but some of the US sites listed are no longer recruiting.

Another trial, "Study of Long-term Safety, Efficacy Tolerability of BYM338 in Patients With Sporadic Inclusion Body Myositis," is being conducted in Boston and Arizona but it is restricted to patients who were in an earlier BYM338 trial.

In both cases, Novartis asks interested patients to call Novartis Pharmaceuticals at 1-888-669-6682.

TMA also has a special forum where those enrolled in a clinical trial can describe their experiences and answer questions. To find the forum, "Clinical Trials," go to www.myositis.org; click on "Community," then "Community Forum."

Save the date!

TMA returns to Orlando for the 2015 Annual Patient Conference, Sept. 10-13, with a full Conference program focused on coping, the latest research, emotional support and all the information you need to live your best life with myositis. The Conference is at Caribe Royale, the fabulous resort that hosted the Conference in 2012. Watch your mailbox for the Conference flyer and plan now to be with us in Orlando!

Find an event

Wanting to join a support group in your area but not sure where to start? Find meetings near you at TMA's website: http://www.myositis.org/event-calendar, or go to the website at www.myositis.org, and click "events" in the top righthand corner.

Looking for a myositis specialist?

Most of TMA's medical advisors see patients. To find their names and contact information, go to TMA's website, www.myositis.org and click on "About TMA" in the lower righthand corner, then select "Medical Advisory Board" from the menu on the right.

You'll also find the full names of staff members, members of the TMA board of directors, and medical advisory board members on page 2 of this publication.

2014 Live Online Discussions

Several times a year, TMA offers live online discussions as a service for TMA members. The discussions are organized around subjects suggested by TMA members and feature members of TMA's medical advisory board and other experts. For those who have never participated, it's easy, and you don't have to be a computer whiz to ask your question. Simply go to www.myositis.org; and find "live discussions" under "My TMA."

As each discussion approaches, we'll let members know, via email, Facebook posts and home-page reminders. If you see you're unavailable at the time of the discussion, there's the option of leaving your question in advance. The medical professionals answering questions will pick the questions of most general interest and answer them during the discussion. If you can join TMA during the actual discussion, you can ask your question simply by typing it in the specified box. That's it! Shortly after the discussion a transcript will be found online with names removed for your privacy. TMA's experts try hard to answer every question that's not a duplicate.

Please take the time to look through the short summaries below for topics of interest to you, and read the whole transcripts of the six 2014 Live Discussions on TMA's website. Please feel free to suggest any topic of interest to you by emailing TMA@myositis.org.

Understanding Autoimmunity - *Dr. Tahseen Mozaffar, director of the Neuromuscular Center at UC Irvine Medical Center*

Dr. Mozaffar answered questions about the connection of autoimmunity with risk factors, celiac disease, statins, fungal infections and hormones. He also responded to questions about treatment with stem cells, prednisone, plaquenil and physical therapy; and responded to the "cleanliness" theory of autoimmunity.

Autoantibodies - *Dr. Mark Gourley, Washington, DC rheumatologist, researcher in myositis studies at the National Institutes of Health*

Dr. Gourley answered questions about myositis syndromes, lung disease, amyopathic dermatomyositis, CPK levels, the body's response to toxins, and statins. He also explained why autoantibodies can change and why scientists are unsure if they are a result or a cause of autoimmune disease.

Exercise - *Dr. Helene Alexanderson, Division of Physical Therapy at Karolinska Institute in Sweden*

Dr. Alexanderson fielded questions about exercising on a treadmill, using light and heavy weights and how often to exercise. She explained the impact of exercise on muscles both while in a flare and in remission, and suggested that exercise at appropriate levels can benefit people in almost every stage of muscle disease.

Rituximab - *Dr. Rohit Aggarwal, Assistant Professor of Medicine and the Education Coordinator for the Rheumatology Division of the University of Pittsburgh Department of Medicine*

Dr. Aggarwal answered questions about timing of rituximab treatment, its compatibility with other drugs, problems with infusion, its expense, and individual indications that rituximab might work. He also wrote about the large Rituximab in Myositis trial and its overall positive results.

Prednisone - *Dr. Mazen Dimachkie, University of Kansas Medical Center, director of the Neuromuscular Section*

Dr. Dimachkie explained the uses and side effects of prednisone and answered questions about tapering and drug interactions. He touched on the use of prednisone in IBM and answered your questions about a "safe" maintenance dose.

Current trials, from page 3

compared to placebo in active DM patients and to determine the minimum dose required for a maximal clinical effect. Domestic centers are now recruiting in California, Arizona, Miami, Massachusetts and Kansas, with more domestic and international centers to open. To be seen at any center, call Novartis Pharmaceuticals, 1-888-669-6682.

Look for updates at www.clinicaltrials.gov for all active studies. Remember to click on "Contacts and locations" to see the drop-down list. Several of these trials are opening new centers.

Follistatin, from page 5

At TMA's Annual Patient Conference, Dr. Zarife Sahenk, Director of the Clinical and Experimental Neuromuscular Pathology laboratory at Nationwide Childrens, confirmed that the other patients in the study also showed improvement in their timed walk, although not as dramatic as Augie, who walked 149 meters further at six months than at baseline. One patient walked 62 meters farther, she said, and the third walked 23 meters farther.

Conference, from page 15

- New approaches to exercise; Lessons from the children - Drs. Helene Alexanderson, Dr. Sue Maillard (slides and video)
- Overlap syndrome - Dr. Christina Charles Schoeman
- Questions and answers about prednisone - Dr. Mazen Dimachkie
- Reports from TMA's Medical Advisory Board (live broadcast)
- Welcome to the 2014 Conference - Bob Goldberg and Augie DeAugustinis

Myositis and infection

In a study published online in *Arthritis Care and Research*, infections were found to be the leading cause of in-hospital death among patients with dermatomyositis and polymyositis.

Among more than 15,000 hospitalizations between 2007 and 2011 for patients with these two conditions, infections were the main predictor of inpatient death, according to Sara G. Murray, MD, of the University of California, San Francisco, and colleagues. Mortality was strongly associated with bacterial infections, particularly pneumonia and bacteremia. Previous small studies have suggested that infections cause considerable morbidity in dermatomyositis/polymyositis, but population-based studies have not yet assessed the true burden or the contribution to mortality.

Murray and colleagues analyzed data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample, which represents about 20% of U.S. hospital discharges. The 15,407 hospitalizations for patients with dermatomyositis/polymyositis were compared with a random sample of hospitalizations among patients without these disorders, which included 27,990 patients.

Disease factors and comorbidities other than infection that were associated with mortality were interstitial lung disease, malignancy, and cardiovascular disease.

Dr. Marvin Lauwasser, an infectious disease specialist and a member of TMA's Board of Directors, made a presentation at TMA's 2014 Annual Patient Conference on autoimmune diseases and infection. Find the video and all the Conference videos linked from TMA's home page, www.myositis.org.