Clinical trial participants push progress forward

Studies present an opportunity to expand our understanding of MS causes and treatments.

by Andrea Sachs

Jeri Burtchell was scared. She wondered whether signing up for a clinical trial was the right thing to do. Even the consent form for it was daunting, she recalls. “It was about 30 pages, and it was all medical and legal language. It wasn’t worded in a way I could understand.”

Nervous about participating in a clinical

trial at first, Jeri Burtchell on was gratified she took the leap.
Photo courtesy of Jeri Burtchell

It was August 2007, and Burtchell, who had been diagnosed with relapsing-remitting multiple sclerosis in 1999, was wracked with uncertainty: “My concern was: What happens to me if I’m on this mystery medicine and I’m left unresponsive, and nobody even knows that I’m on it?”

But after eight years of rocky health and continuing exacerbations on a disease-modifying therapy, the Palatka, Florida, resident decided to trust her new neurologist, who was the lead investigator of the study, and take a chance.

Once she showed up for the first appointment, Burtchell’s fears were calmed. She learned that, according to the Food and Drug Administration, a study investigator must be readily available by phone or electronic communication 24 hours a day throughout the study, and within reasonable travel distance to study participants, particularly if there are concerns about toxicity. The FDA says study participants must also be clearly educated about the possible need for such contact and precisely how to obtain it. In addition, Burtchell learned, investigators or their associates are generally available to answer any questions that arise, whether about the consent form or anything that happens during the trial.

Burtchell began to take the experimental medication, which was provided free but would have run thousands of dollars a month if purchased at a pharmacy—the first of many benefits she saw. The former printer and graphic artist began to blog about her experience: “If this gets approved, I’m in heaven!”

It’s a phase

Before evaluating a potential treatment or device for approval, the Food and Drug Administration requires that each undergo a clinical study, in three carefully monitored stages. Here is what is involved in each phase of an MS-related clinical trial:

Phase 1

This phase involves a small number of people (usually no more than 80), who may have MS or who may be healthy, who are tested for the safety of the agent. This usually takes several months.

Phase 2

This stage generally lasts several months to two years and often involves hundreds of people with MS. This phase helps determine whether the treatment is safe and shows sufficient effectiveness to pursue in larger, longer studies.

Phase 3

This full study, often with many hundreds of participants at multiple sites, seeks to understand the benefits and side effects of the treatment. This phase often takes two to four years. The FDA often requires two phase 3 studies to evaluate a new therapy.

Fast forward to 2014: Like most study participants, Burtchell wasn't told whether she was taking the experimental medication or an already approved medication; however, she says that after starting the clinical trial she didn't have another relapse for six years.

"It made such an astounding and dramatic difference in my life, in who I was, and how I could get back to a sense of normal." She continues to take the medication, which is now on the market, in part because of the research she participated in. Of course, people respond to medications differently, which is among the reasons it's so important that there be as many treatment options as possible for people with all forms of MS.

Experts caution that not all trials end up with such Hollywood endings—sometimes medicines don't work, or even worse, have side effects that bring the trial to a halt. In addition, while in most instances, the research team covers the cost of the study drug and any medical care performed to fulfill the study's goals, it's still wise for participants to contact their health insurers—with the protocol or informed consent form in hand—to understand fully what they might be expected to pay.

Some clinical trials don't test drugs; rather, they evaluate diagnosis and rehabilitation strategies, or perhaps factors that contribute to disease progression.

Uphill journey

Prospective medications must travel a long road before they have a chance at being marketed to the public. The FDA carefully monitors clinical trials. All study participants must sign a consent form that details the purpose of the trial, the procedure schedule, and the known possible risks and benefits. The FDA then requires all studies to complete three carefully monitored stages before it will evaluate an agent or device for approval. (See sidebar at right.) The FDA review process can take 10 months or longer. Completing all the required phases of a clinical trial can take years.

It's crucial for participants to understand what the treatment being studied in a phase 2 or 3 trial is being compared to, such as another treatment or an inactive placebo. Treatment options—particularly for relapsing forms of MS—are available, so participants must understand what their options are and what the probability is
of receiving the placebo.

Pharmaceutical companies are the main source of funding for large-scale phase 3 drug trials, which can cost up to $100 million to conduct. Other sponsors of drug and research studies include universities and the federal government. The National MS Society is another pivotal participant in the advancement of research and clinical trials. The Society is currently supporting approximately 30 clinical trials of potential treatments or rehabilitation interventions for MS, and devoted nearly $50 million last year to a spectrum of key initiatives and other research projects. It's a steep hill to climb: Only 8 percent of drugs that enter phase 1 studies ever reach the market, according to the FDA.

As a result of the Affordable Care Act, the FDA is now mandated to consider "patient-centered outcomes" in judging the effectiveness of drugs, in addition to their scientific properties. That makes the subjective reactions of thousands of participants in clinical trials of MS medications, and their quality-of-life concerns, increasingly relevant, says Dr. Bruce F. Bebo Jr., the associate vice president of discovery research for the Society. "It is critically important that we capture the patient's perspective."

The circle widens

Clinical trials were for a long time conducted almost exclusively with Caucasians due to low minority enrollment. Ethnic diversity has become a new focus to ensure that the safety and effectiveness of treatments is studied in all people. "Over the past 10 years, there has been increasing interest in examining the characteristics of MS in minorities, including African-American, Hispanic and Asian populations," says Dr. Mitzi Williams, a neurologist at the MS Center of Atlanta.

However, Dr. Gary Puckrein, president of the National Minority Quality Forum, reports that "historically, our clinical trial ecosystem has had trouble getting diverse populations into clinical trials." According to his organization, only 5 percent of current participants are black, and only 1 percent are Hispanic. In the African-American community, there has been particular apprehension about such tests, because of serious ethical lapses that occurred almost half a century ago during an infamous clinical trial conducted by the Tuskegee Institute in Alabama between 1932 and 1972 on African-American men.

Today's lack of diversity may be affecting study results and possibly preventing people from getting the treatment they need, says Dr. Williams. The limited studies that have focused on African-Americans suggest that this population may have more aggressive forms of MS, characterized by more MRI lesions, earlier onset of walking disability, and more frequent involvement of their optic nerves and spinal cords. In addition, limited research shows that Asian-Americans tend to have more opticospinal disease (where the MS lesions are more concentrated in the optic nerves and the spinal cord than the brain, so people have more visual and walking symptoms).

Hispanic-Americans seem to have an earlier age of onset, and present with optic neuritis or spinal cord symptoms, but they don't appear to have earlier walking disability compared to their Caucasian counterparts, Williams says.

So it’s possible that MS therapies may work differently among diverse ethnic and racial groups, but these differences are difficult for researchers to tease out if there are not enough participants from these groups involved in the phase 3
clinical trials.

Thanks to a clinical trial, Gale Loving learned that her optic neuritis was due to MS.
Photo courtesy of Gale Loving

Gale Loving, an African-American woman in Chicago who participated in a clinical trial for optic neuritis, found out from the study that her optic neuritis was due to MS, and once diagnosed, received the treatment she needed. “I feel very blessed that I was in that study,” she says.

Loving is now an enthusiastic booster of taking part in research studies: “It wasn’t painful,” she says. “It was just the gathering of knowledge.”

More than anything else, volunteers with MS are met with gratitude. “Anybody who participates in a clinical trial should feel like he or she has made a tremendous contribution; it’s one of the more personal and impactful contributions a person can make,” says Dr. Bebo. “Big clinical trials, whether they have promising outcomes or not, are some of the milestones we’ll look back on as significant progress toward finding solutions for MS.”

Taking part
Study participants have different motivations for getting involved, says Dr. Anne Cross, a professor of neurology at the Washington University School of Medicine in St. Louis, who has run 25 MS-related clinical trials. “Maybe what they’re taking right now is not working really well, and they want to try something different, and this is a way to get something different

much more quickly than waiting for it to be FDA-approved," she says. "Another reason is to help with scientific advancement; they want to do something altruistic for the world and for their fellow [members of the MS community]. And then there are other people who do it because it is a way for them to get free medicine for their MS."

Everything possible is done to ensure patient safety during a clinical trial. Participants are asked at the beginning of a study about any medications they are taking and about their general health in order to avoid any possible complications. They're informed of all known risks and are also told, sometimes to their surprise, that they can leave a study at any time, though researchers obviously hope that they won't.

Nevertheless, risks are present. Midway through Burtchell's trial, she and her fellow participants were informed that two people in the study had contracted viruses and died. Participants were then tested to make sure they were not vulnerable to the same illness. "I was terrified," says Burtchell, "but the medication was working well for me. I was more afraid of having my MS symptoms return [than of the possible side effects]."

Interested in taking part in a clinical trial?

The following websites will point you to studies near your home:

- nationalMSsociety.org
- clinicaltrials.gov
- centerwatch.com

For a list of questions to ask before agreeing to participate in a clinical trial, visit nationalMSsociety.org/clinicaltrialFAQ.

Such a decision will be different for every individual, but after talking at length with the researchers (including her own neurologist), Burtchell decided to continue with the study. She was monitored very closely; the first time she took the investigational drug was at a clinic, where she was observed for the next six hours. When no adverse effects were seen, she was able to take it on her own thereafter, with
the knowledge that she could reach out to the researchers at any time.

Being in a clinical trial also can involve a substantial time commitment. Loving's study on optic neuritis initially meant going to a hospital four times a year for hours of eye tests. There were also neurological tests, and an MRI once a year.

In Burtchell's case, the consequences of participating were not only time-consuming, but unpleasant. So that she and her doctor wouldn't know which experimental group she was in (as a way to control bias that could impact the study results), she was required to take weekly shots as well as a pill every day. "It was a two-inch needle in my thigh. I didn't enjoy it

at all.” Despite these tribulations, Burtchell has since become a passionate advocate for taking part in clinical trials: “If we want a cure, we have to be willing to be involved in the research.”

Andrea Sachs is a New York City-based journalist who was diagnosed with MS in 2009. She recently took part in two non-drug clinical trials and says the experiences were rare opportunities to contribute to creating a world free of MS.

Considering participating in a clinical trial? Be sure to discuss it first with your healthcare provider.

To learn more about participating in clinical trials, see the National MS Society’s Clinical Trials Guide.