

## Glimmers of hope for people with progressive MS

by John R. Richert, MD

Last fall's publication of results from a large-scale clinical trial of the drug rituximab (Rituxan, Genentech and Biogen Idec) brought glimmers of hope to prospects for treating progressive MS—even though, for the most part, the drug failed its primary objective of slowing disease progression in people with the primary-progressive form of MS.

The trial was designed to explore both the primary end point of disease progression, and also some other endpoints, and to analyze effects in several specific subgroups. What the trial found was telling.

Those on Rituxan therapy had significantly smaller increases in the volume of their brain lesions after 96 weeks. Analyses of subgroups showed that disease progression was significantly delayed in those who were less than 51 years of age and in those whose pre-treatment MRIs showed signs of active (gadolinium-enhanced) brain lesions. These enhanced lesions are indicative of active inflammation.

There's been ongoing debate about the extent to which inflammation plays a role in primary-progressive MS. These results offer new evidence that a possibly substantial subgroup of

younger people with primary-progressive MS may benefit from anti-inflammatory therapy.

There are other clinical trials planned or in progress focusing on progressive MS. One is a large-scale trial of oral fingolimod from Novartis. They also offer hope that a specific therapy for progressive MS may be forthcoming at last.

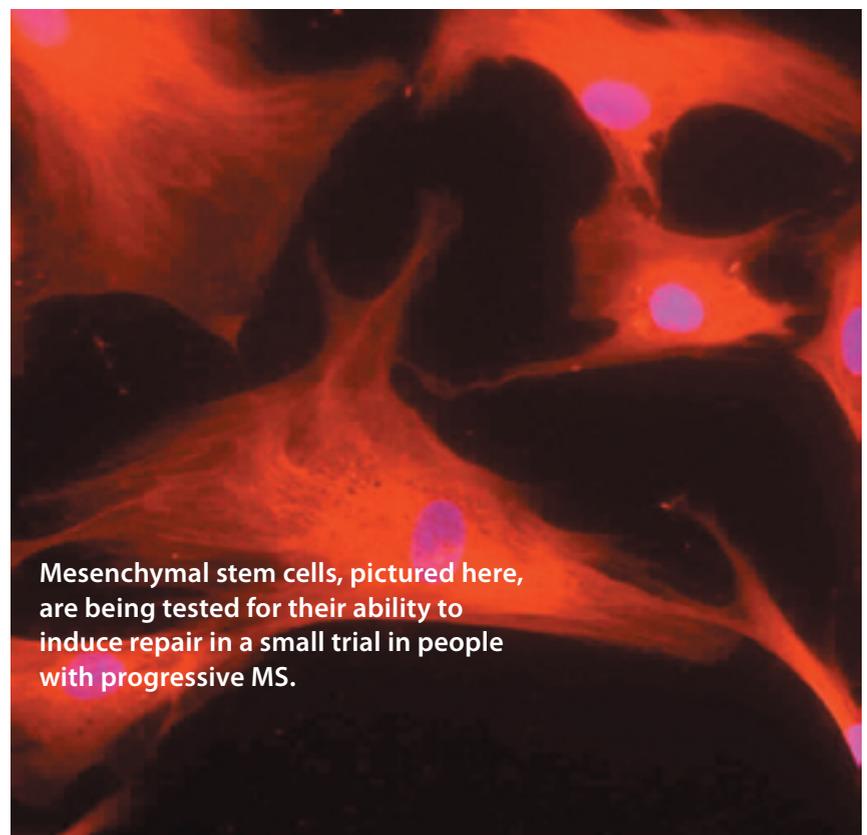
Other projects of particular relevance include efforts to protect nervous system tissues (called neuroprotection) and studies aimed at reversing damage and restoring function. Restoring function can range all the way from research into rehabilitation techniques to experimental stem cell therapies.

You'll read about one approach to restoring function in this issue of Research Now. (See "Investigating ion channels for MS symptoms, and even neuroprotection" on page 61.)

On the rehabilitation side

A new project by Dr. Victor Mark, of the University of Alabama at Birmingham, is testing a type of physical therapy that has been successfully used in people recovering from stroke. "Constraint-Induced Movement therapy (CI therapy)" involves using a person's weaker arm to do skilled movements to promote increased use of that limb in daily life. Dr. Mark's clinical trial will randomly assign people with progressive MS either to CI therapy or to complementary and alternative treatment to provide new understanding of the potential of this approach.

One possible factor in causing



Mesenchymal stem cells, pictured here, are being tested for their ability to induce repair in a small trial in people with progressive MS.

FIGURE PROVIDED BY PROFESSOR NEIL SCOLDING, UNIVERSITY OF BRISTOL, UK.



**Here, an individual who experienced a stroke is practicing constraint-induced therapy, which encourages use of the weaker limb to promote its increased use. A team at University of Alabama Birmingham is testing this therapy in people with progressive MS.**

nervous system damage during the course of MS is a molecule called glutamate. It helps excite nerve cells, but too much of it may contribute to injury. With Society funding, Dr. Emmanuelle Waubant of the University of California, San Francisco, is conducting a clinical trial to see whether oral riluzole (a drug approved for treating ALS) can prevent the release of glutamate and, it is hoped, protect nerve fibers from damage in MS. Although this study involves people recently diagnosed with relapsing MS, its results will have implications for people with progressive MS as well.

Another neuroprotective agent being tested in relapsing forms of MS that may also impact people with progressive MS is the antibiotic minocycline. Trials are getting underway with the aim of stopping or slowing disease progression.

A key mission of the four international teams involved in the Society's Nervous System

Repair and Protection initiative (supported through the Promise: 2010 campaign) is to lay the groundwork for clinical trials to protect the nervous system and restore function. Now in their fifth year, these investigators have some trials that are already underway or in planning stages.

Team leader Dr. Gavin Giovannoni, of Queen Mary University of London in the UK, has been involved in a large multicenter study investigating whether the active compound in cannabis, called THC (tetrahydrocannabinol), is neuroprotective and can slow MS progression.

Two of the other repair teams are about to launch new, small-scale clinical trials with separate funding. One will investigate the safety of treatment with bone marrow (mesenchymal) stem cells; the other will attempt injections of neural stem cells. Both trials are fully enrolled and awaiting further funding and approvals.

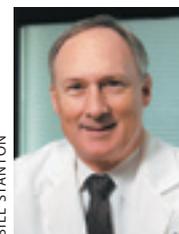
Despite these challenging economic times, we've just committed to funding four new Collaborative MS Centers, two of which are focusing on nervous system repair.

The Center led by Dr. Thomas Lane at the University of California at Irvine is exploring the potential of stem cells for stopping disease progression and restoring function. The new Center led by Dr. Moses Rodriguez at Mayo Clinic is zeroing in on molecular signals that might stimulate—or inhibit—repair processes in MS. His team is seeking clues to developing therapeutic strategies to promote repair.

All told, the Society has over \$40 million committed to new and ongoing projects focusing on approaches to repair damage or restore function. This is a high-priority investment, and it's beginning to pay off.

To read more about all of our Centers, go to [nationalMSSociety.org/research/research-we-fund/collab-research-centers/index.aspx](http://nationalMSSociety.org/research/research-we-fund/collab-research-centers/index.aspx).

To read more and view videos about living with progressive MS, go to [nationalMSSociety.org/living-with-multiple-sclerosis/progressive-ms/index.aspx](http://nationalMSSociety.org/living-with-multiple-sclerosis/progressive-ms/index.aspx). ■



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