Providence MS

What is Active Secondary Progressive Multiple Sclerosis?

Written by Elisabeth Lucassen, M.D.

In Spring of this year, the FDA approved two new medications for patients with a specific type of multiple sclerosis. The disease modifying therapies Mavenclad (cladribine) and Mayzent (siponimod) were already approved for Relapsing Remitting Multiple Sclerosis (RRMS). The FDA's recent decision means they are now approved for active Secondary Progressive Multiple Sclerosis (SPMS). So what does this mean for patients?

For most patients, multiple sclerosis begins as RRMS. During this time, relapses and active inflammation show up as contrast enhancing lesions on MRI scans. Over time though, the disease transitions into a more neurodegenerative stage called SPMS. Relapses may still be possible during this stage, but they are certainly fewer. Many patients during this stage describe worsening symptoms, such as trouble with walking or cognition, but no new lesions appear on MRI scans. Since MS specialists currently have no validated measures to confirm this stage of disease, they usually make a clinical diagnosis several years after the onset of progressive symptoms.

MS specialists used to think the disease modifying therapies available for RRMS were not as helpful in SPMS due to clinical trials that showed negative or conflicting results. But our understanding of the MS disease process evolved, and so did our definitions for RRMS and SPMS. We now understand that these are not static designations, and that the transition from RRMS to SPMS can happen gradually over many years. We also now know that controlling MS in the early RRMS stage may influence whether there will be a transition to a typical SPMS disease course and how long it may take to get there. So, we want to treat early and treat effectively, in order to have the best possible outcomes for the long term.

“Active SPMS” is a newer designation. It comes from a reclassification of MS subtypes in 2013, which happened because our understanding of MS and its pathology increased. We now recognize that both the inflammatory disease seen with RRMS, and the neurodegenerative disease seen with SPMS can occur simultaneously for some time. So if a patient comes in for an exam and has both the gradual worsening we associate with SPMS as well as new MRI lesions or relapses, they have active SPMS.

More recent research is helping us understand the underlying disease process in progressive MS, as well as the transition from RRMS to SPMS. One study discovered a method to detect slowly expanding/evolving lesions (SEL) on MRI in both RRMS and Primary Progressive MS patients. This correlates with the “smoldering plaques” that are common in progressive MS patients. “Smoldering plaques” are older lesions that slowly evolve over the long term and result in axonal damage and demyelination. These plaques are mainly seen in patients who have had MS for more than 10 years, and they peak in patients who have had MS for more than 20 years who are also over age 50. Basically, this study found that RRMS patients can have SELs, but that PPMS patients have significantly more. The study also noticed that the characteristics of these lesions change over time. The authors concluded that their new detection method could be a way to see chronic active MS lesions on MRI scans. In other words, it might be a biomarker for smoldering inflammation in MS.

We are starting to understand more about progressive MS, but there are still many questions for researchers to answer. We hope to develop better clinical tools that will help us define the transition between different MS subtypes over time. Some large research studies are using blood and spinal fluid biomarkers to improve...
Interview with Justine Brink, D.O., M.P.H.

Where did you complete your training?
Undergraduate- Drexel University, Philadelphia, PA.
Medical School- Philadelphia College of Osteopathic Medicine.
Residency- University of Connecticut.
Fellowship and MPH- Thomas Jefferson University, Philadelphia, PA.

Why did you choose to move to Portland?
Music, skiing, coffee, Powell’s Books and the opportunity to join one of the most vibrant MS Centers in the western United States.

How did you become interested in multiple sclerosis?
I became interested in MS through my outpatient clinic in residency. I had several patients with MS with whom I really connected. I knew I wanted a career in a specialty where I would have long term relationships with my patients. At the time, the market was (and still is) exploding with new MS treatment options in large part thanks to centers like this which participate in clinical trials.

What is one piece of advice you would like to give to patients with MS?
Maintain as much independence as possible, but never feel ashamed to accept help when it is offered with love and selflessness.

What is one piece of advice you would like to give to caretakers?
It is okay to step away and take time for yourself. In fact, you need to do that sometimes, because burnout is real. You cannot pour from an empty cup.

What do you like to do outside of work?
Running, skiing, music, poetry and literature.

What do you think will be the next major advance in MS treatment?
Remyelination therapies.

Who would you invite to your dream dinner party (alive or dead)?
George Carlin and Carl Sagan.

What has been the highlight of your career?
I started a Neurology clerkship for the University of Nevada Reno, School of Medicine. The highlight for me was when my first medical students matched into Neurology residencies.

What life experience has taught or changed you the most?
Other than the process of becoming a physician, the two years I spent as a Peace Corps Volunteer in Swaziland (2005-2007) as an HIV/AIDS education volunteer.

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this process and to characterize the inflammatory characteristics in each subtype. As we start to better understand these nuances in the MS spectrum, we will hopefully improve our treatments and care for our patients, which is always the ultimate goal.

References:
Clinical Studies | Enrollment

For more information or to connect with the contacts for any of these trials, please call Jennifer Geranios at 503-216-2736.

Evaluating the Potential Role of Melatonin in Subjects With Relapsing Multiple Sclerosis

**Description:** To date, there is no published data on the role of melatonin supplementation or the appropriate dosage for patients with multiple sclerosis. Because of the potential benefits of melatonin, this pilot study will be an exploratory investigation to evaluate the effect of supplementing melatonin in subjects with multiple sclerosis who are taking an oral disease modifying therapy (DMT) for 6 months or longer. It is our intent that the results of this study will support the rationale and be a prelude to a larger trial which can focus on clinical efficacy of melatonin therapy outcomes.

**Sponsor:** Providence Health & Services  
**Principal Investigator:** Kyle E Smoot, M.D.  
**Contact:** Hannah Voss

Traditional versus Early Aggressive Therapy for Multiple Sclerosis (TREAT-MS) Trial

**Description:** The Traditional versus Early Aggressive Therapy for MS (TREAT-MS) trial is a pragmatic, randomized controlled trial that has two primary aims: 1) to evaluate, jointly and independently among patients deemed at higher risk vs. lower risk for disability accumulation, whether an ‘early aggressive’ therapy approach, versus starting with a traditional, first-line therapy, influences the intermediate-term risk of disability, and 2) to evaluate if, among patients deemed at lower risk for disability who start on first-line MS therapies but experience breakthrough disease, those who switch to a higher-efficacy versus a new first-line therapy have different intermediate-term risk of disability.

**Sponsor:** PCORI (Patient-Centered Outcomes Research Institute)  
**Principal Investigator:** Elisabeth Lucassen, M.D.  
**Contact:** Will Stott

North American Registry for Care and Research in Multiple Sclerosis (NARCRMS)

**Description:** The North American Registry for Care and Research in Multiple Sclerosis (NARCRMS) is a physician/clinician based registry and longitudinal database of clinical records and patient-centered outcomes.

**Sponsor:** Consortium of MS Centers (CMSC)  
**Principal Investigator:** Stanley Cohan, M.D., Ph.D.  
**Contact:** Lynette Currie
Measurement of Relaxin in the Serum and Cerebrospinal Fluid of Subjects With and Without the Relapsing Form of Multiple Sclerosis

**Description:** This study will evaluate relaxin levels in patients with multiple sclerosis.

**Sponsor:** Providence Health & Services  
**Principal Investigator:** Stanley Cohan, M.D., Ph.D.  
**Contact:** Hannah Voss

Multi-center, Randomized, Double-blinded Assessment of Tecfidera® in Extending the Time to a First Attack in Radiologically Isolated Syndrome (RIS) (ARISE)

**Description:** The purpose of this study is to systematically study the efficacy of Tecfidera in those individuals who possess incidental white matter anomalies within the brain following a MRI study that is performed for a reason other than for the evaluation of MS (multiple sclerosis)

**Sponsor:** University of Texas Southwestern Medical Center  
**Principal Investigator:** Stanley Cohan, M.D., Ph.D.  
**Contact:** Abigail Kernan-Schloss

Long-term, Prospective, Multinational, Parallel-cohort Study Monitoring Safety in Patients With MS Newly Started With Fingolimod Once Daily or Treated With Another Approved Disease-modifying Therapy (PASSAGE)

**Description:** The purpose of this world-wide prospective parallel-cohort study in patients with relapsing forms of Multiple Sclerosis, either newly treated with fingolimod or receiving another disease-modifying therapy, is to further explore the incidence of selected safety-related outcomes and to further monitor the overall safety profile of fingolimod under conditions of routine medical practice.

**Sponsor:** Novartis  
**Principal Investigator:** Stanley Cohan, M.D., Ph.D.  
**Contact:** Lynette Currie

A Randomized, Double-Blind, Placebo-Controlled, Multiple Dose Study to Assess the Safety and Efficacy of Elezanumab When Added to Standard of Care in Relapsing Forms of Multiple Sclerosis

**Description:** The purpose of this study is to evaluate the safety and efficacy of elezanumab in subjects with relapsing Multiple Sclerosis (RMS).

**Sponsor:** AbbVie Inc  
**Principal Investigator:** Kyle E Smoot, M.D.  
**Contact:** Genevieve Rollier
Evaluating the Efficacy and Safety of Transitioning Patients From Natalizumab to Ocrelizumab (OCTAVE)

**Description:** The primary objective of this study is to assess the efficacy of Ocrelizumab (OCR) in Relapsing Multiple Sclerosis patients who have been previously treated with natalizumab (NTZ) by evaluating relapse rate, progression on MRI and disability progression.

**Sponsor:** Providence Health & Services  
**Principal Investigator:** Kyle E Smoot, M.D.  
**Contact:** Genevieve Rollier

A Randomized, Double-Blind, Placebo-Controlled, Multiple Dose Study to Assess the Safety and Efficacy of Elezanumab When Added to Standard of Care in Progressive Forms of Multiple Sclerosis

**Description:** The purpose of this study is to evaluate the safety and efficacy of elezanumab in subjects with progressive Multiple Sclerosis (PMS).

**Sponsor:** AbbVie Inc  
**Principal Investigator:** Stanley Cohan, M.D., Ph.D.  
**Contact:** Genevieve Rollier

Pacific Northwest Multiple Sclerosis Registry

**Description:** The purpose is to measure MS prevalence in the Pacific Northwest and to create a database for ongoing epidemiological and health services research.

**Sponsor:** Providence Health & Services  
**Principal Investigator:** Stanley Cohan, M.D., Ph.D.  
**Project Manager:** Tamela Stuchiner

Providence Ocrelizumab Patient Registry

**Description:** The goal is to collect information from patients receiving ocrelizumab for the treatment of MS to assess its long term utilization, safety, tolerability and efficacy.

**Sponsor:** Providence Health & Services  
**Principal Investigator:** Kyle Smoot, M.D.  
**Study Coordinator:** Lois Grote
A Systems Approach to Understanding Disease Processes in MS

Description: The main purpose of the study is to improve the understanding of MS and to look at the genetic factors that may influence how MS progresses. This study will collect blood and stool samples and information from survey questions and MS-related assessments from study patients over 15 months of study participation.

Sponsor: Providence Health & Services
Principle Investigator: Stanley Cohan, M.D., Ph.D.
Study Coordinator: Will Stott

For more information on clinical trials and research, visit us at oregon.providence.org/our-services/c/clinical-trials-brain or clinicaltrials.gov
Providence Multiple Sclerosis Center

Providence Multiple Sclerosis Center, the only center of its kind in Oregon, is the state’s leading care provider for people with MS. Our medical director, Stanley Cohan, M.D., Ph.D., was an investigator in the original, pivotal trial of beta interferon 1-A, one of the key medications for treating multiple sclerosis. He continues to play a leading role in MS research and founded the Pacific Northwest Multiple Sclerosis Registry Project, which will be used to help advance treatment of multiple sclerosis.

Our goal at Providence Multiple Sclerosis Center is to provide persistent, proactive, focused treatment that minimizes the effects of MS on your life. Patients benefit from comprehensive services that may include medication therapy, physical rehabilitation, counseling and other support. In addition, patients have access to the newest therapies through regional and international clinical trials.

**Our Providence Multiple Sclerosis Center team specializes in:**

- Comprehensive MS care
- Neurology
- Neuro-opthalmology
- Nursing
- Physical therapy
- MS research
- Support and wellness programs

**OUR CLINICIANS:**
Stanley Cohan, M.D., Ph.D., Neurologist, Medical Director of Providence Multiple Sclerosis Center
Justine Brink, D.O., M.P.H., Neurologist
Vitalie Lupu, M.D., Neurologist
Kiren Kresa-Reahl, M.D., Neurologist
Elisabeth Lucassen, M.D., Neurologist
Kyle Smoot, M.D., Neurologist
Leah Gaedeke, F.N.P., Multiple Sclerosis Nurse Practitioner

**OUR NURSES:**
Sam Brighton, R.N., B.S.N., Clinical Case Manager
Kiana Oskooi, R.N., B.S.N., Clinical Support Specialist
Kimberly Tracyk, R.N., B.S.N., Clinical Support Specialist
Nora Vetto, R.N., M.S.N., Clinical Support Specialist

**OUR SERVICES:**
- Highly advanced diagnostics
- Personalized treatment plans
- Attentive use of medications
- Rehabilitation with therapists who specialize in MS care
- Continence treatment for bladder and bowel dysfunction
- Emotional support and psychological counseling
- Opportunities to receive investigational medicines through clinical trials
- Close coordination with your primary care physician
- The Pacific Northwest Multiple Sclerosis Registry Project, a database created for epidemiological and health services research
- An MS Network that allows physicians to collaborate on MS treatments
- Community and provider education forums throughout Oregon

Thanks to clinical research, people with MS are living longer, stronger, healthier lives.

Available on our Web site at providence.org/brain:

• **Physician directory:** Get contact information for all Providence Brain and Spine Institute physicians.

• **Upcoming events:** Providence offers educational events throughout the year. Check our online calendar to view upcoming topics.

• **Clinical trials:** Find out about multiple clinical trials for investigational treatments for MS, as well as other clinical trials available through Providence.

• **Support groups:** Get details on support groups in Oregon.

• **Additional resources:** Our website offers the latest information on available programs and services; educational toolkits; and links to trusted sources of information.

News & Events:

• The MS Support Group meets for lunch from noon-1:00 p.m. on the first Thursday every month. Springwood Conference Room: Providence St. Vincent Medical Center, Mother Joseph Plaza. Lunch is provided.

• Join us for Multiple Sclerosis 101, a free educational program for newly diagnosed patients. Our next MS 101 with Dr. Kyle Smoot is on Thursday 11/7 at 6:00 p.m. at Providence St. Vincent Medical Center. Register at providence.org/classes.

• Dr. Kyle Smoot is available to see patients on the East Side every Friday. For more information, contact Providence Neurological Specialties East at (503) 215-8580.

Ocrelizumab was FDA approved last year and goes by the name Ocrevus. It’s been described by some as a ‘game-changer’ in the battle with MS. I’m proud of the fact that I was part of something that stands to help 100’s of thousands of those afflicted.

My new normal is that I forget I have MS until my next six-month infusion and I have to smile.

— Jeff R.

**The New Normal:**

After the initial fear and shock of being told I have MS back in 2012 my life is now back to what I call the ‘New Normal’. I was diagnosed with RRMS and lucky enough to be referred to Dr. Kyle Smoot at Providence Neurological Specialties and be offered to participate in a double-blind Phase III trial of a promising MS drug-seeking FDA approval by the name of Ocrelizumab that Dr. Stanley Cohan was overseeing. My initial response was skepticism with a dash of curiosity. However, both specialists answered my questions and raised points I didn't even think to ask alleviating my worries.

After some research of my own, I opted to participate in the study and started in earnest early in 2013. This was likely one of the most fortuitous decisions I have ever made. Not only did I get excellent care, extensive testing and MS drug treatment at no cost, but I’ve made what I would consider new friends during my time in the study.

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