THE POWER OF PATIENTS

Informing Our Understanding of Rare Diseases
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Informing Our Understanding of Rare Diseases
Foreword

There are approximately 7,000 rare diseases affecting an estimated 30 million people in the United States. In the vast majority of these cases, an FDA-approved treatment for a rare disease indication will be altogether lacking, and physicians, who may encounter one or two such patients in the course of their careers, will typically have to rely on trial-and-error approaches, along with their own intuition, to provide care. We often hear that the paucity of medical products on the market for rare diseases reflects economic pressures that drive developers to invest their resources into more prevalent diseases, where the financial payoff for new drug development is potentially greater and more immediate. But the tremendous medical need that remains unmet today within the collective rare disease community, in fact reflects a fundamental truth about rare diseases that goes beyond economics. By their very definition, rare diseases may be difficult to localize and subject to converted methods of investigation, creating huge barriers to understanding for stakeholders who might otherwise define and pursue opportunities for developing new therapeutics. This problem has been central to the collaborative efforts between the FDA and NORD for many years. The very gratifying progress that we’ve seen in surmounting hurdles to the understanding of rare diseases is evidenced in the NORD natural history registries discussed in the following chapters.

The “natural history” contained in the registries NORD has compiled within the organization’s IAMRARE® program, represents the enactment of strategies to harness the very type of knowledge so essential for the design and execution of clinical trials of potential new therapies, but which has been lacking in the rare disease space. This natural history information is built on the unique insights of those patients living with rare disease. At the FDA, we have found in our patient-focused drug development meetings—for example, with people living with chronic disease—that patients really are the experts in their particular disease. They may not know all the medical jargon and all the laboratory terms familiar to medically trained professionals, but their expertise, built on their experience of living day-in and day-out through the course of their disease, is the cornerstone of the natural history contained in the NORD registries presented in this volume. This information encompasses how these diseases progress over time, what symptoms may occur and how these might be measured, how many patients may be expected to develop the disease, and how patients may have responded, both positively and negatively, to various treatments.

Knowledge of the natural history of rare diseases informs the design of efficient clinical trials in many ways, helping reduce the length and cost of drug development and contributing toward greater predictability of clinical development programs. But in addition to the natural history information they contain, natural history registries also subserve the enormous benefit of enabling people with rare diseases to find each other and to come together to access their collective experience. Additionally, drug developers who are planning clinical trials often consult with patients with the disease to be targeted, who may best know what is feasible to do in a clinical trial, what might not work for certain patients, and may even be able to suggest patients for a trial or participate themselves. If patients aren’t consulted in a good part of the trial design process, we frequently end up with clinical trials that are weakened, with multiple patient enrollee drop-outs, because people find they can’t participate in a trial that has not been suitably designed.

A great deal of useful information, very valuable to the work the FDA does in the rare disease space, can come from patient registries and from having patients robustly participate and share information about their disease, among themselves and with their caregivers and clinicians. Patient input drives the collection of natural history information and is the basis for the considerable success of the NORD registries program, complementing the FDA’s work in bringing new therapeutics into clinical use. On behalf of the FDA, I encourage people who are touched by rare disease to participate in the development of these registries and in the initiation of those yet to come.

Janet Woodcock, MD
Director
Center for Drug Evaluation and Research
US Food and Drug Administration
Who we are

The National Organization for Rare Disorders (NORD®) is the leading independent advocacy organization representing all patients and families affected by rare diseases. NORD is committed to the identification, treatment and cure of the more than 7,000 rare diseases, of which approximately 90% are still without an FDA-approved treatment or therapy.

The organization began as a small group of patient advocates that formed a coalition to unify and mobilize support to pass the Orphan Drug Act of 1983. For more than 35 years, NORD has been leading the fight to improve the lives of patients with rare disease by supporting patients and organizations, providing education, driving public policy, advancing medical research and providing patient and family services for those who need them most. NORD is made strong together with more than 280 disease-specific member organizations and their communities. NORD also collaborates with many other organizations on specific causes of importance to the rare disease patient community.

Patient-powered natural history studies are transforming how patients and caregivers inform and shape medical research and translational science for rare diseases. After a multi-year planning process, NORD developed and launched our IAMRARE registry program in 2014. This was done with guidance from patients, caregivers, researchers, and clinicians, as well as key opinion leaders from regulatory agencies, including the FDA and the NIH, to address persistent knowledge gaps and promote equitable and sustained progress on rare disease research. NORD’s registry program unites the rare disease community on a common data collection platform that supports research-grade, longitudinal, patient-experience natural history data.

By bringing interdisciplinary teams together, NORD has created a successful model of developing patient-driven research outlets that complement clinical data sources. NORD takes a multidisciplinary approach to supporting research efforts through the development of consortia, partnering with different stakeholders to accelerate the generation of data, translating findings to inform meaningful outcomes, and providing pathways for the dissemination of information within the rare disease and broader health communities.
Trio Health is pleased to offer our team and capabilities to assist NORD and its member organizations in the pursuit of their mission to identify, treat, and cure patients with rare disorders.

The mission of Trio Health, founded in 2013, is to collect and analyze real-world evidence that may be used to improve the quality of health care available to all patients. We achieve our mission by understanding not only the patient, but also the “trio” of other stakeholders—physician, pharmacy, and insurance company (payer)—and by evaluating how each clinical decision and the workflow have an impact on the overall care of the patient.

Our approach to real-world evidence is predicated on 3 factors: high-integrity data, the right statistical approach to analyze the data, and study conclusions without bias.

To build a high-integrity disease database requires that Trio combine disparate data from each patient stakeholder to form a 360-degree view of the patient. Cross referencing each data source to validate and track the patient journey is unique to Trio Health. Since each patient has his or her own clinical story, our collaboration with each of the patient stakeholders provides unparalleled insight.

To ensure that Trio publishes without bias, Trio retains an independent Scientific Steering Committee (SSC) for each disease that collaborates with our analytics team to author all studies. Sponsorship of each study by a pharmaceutical company, payer, or health plan is classified as investigator-sponsored research (ISR) to prevent any bias from the sponsor of the study. We thank and greatly appreciate all of our partners who respect and support our methodology.

High-integrity real-world evidence will play an important role in establishing the equilibrium between the competing forces among all of the patient stakeholders. Physicians, pharmacies, pharmacy benefit managers, payers, and pharmaceutical companies all share a common goal to provide the right treatment to the right patient. Trio’s position is that real-world evidence provides the path to achieve this goal.

If the patient wins, all stakeholders will achieve clinical excellence.
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OMS
Opsoclonus-Myoclonus Syndrome

OMSlife Foundation

REGISTRY POWERED BY NORD
Alexa's battle began in the fall of 2009 at the age of 15 months. She toddled to bed one evening and did not walk again for months. During the early stages of illness, Alexa lost her ability to walk, sit, talk, and even hold objects. Her parents took her to various doctors and specialists, but no one had an definitive answer for the rapid deterioration of Alexa's health. Despite continuous efforts, her family was unable to find any diagnosis for Alexa's condition.

Finally, at the age of 8 years old, Alexa had her last MRI treatment, and her parents were informed that Alexa had OMS. They founded the OMSLife Foundation in 2012 to provide information and be a resource; the foundation now serves more than a thousand patients throughout the world. Our mission statement is "to raise awareness, fund research, and help others." OMSLife is a nonprofit organization founded in 2012 to provide information and be a resource; the foundation now serves more than a thousand patients throughout the world. The foundation statement is "to raise awareness of Opsoclonus-Myoclonus Syndrome, fund research for patients and caregivers, and raise funds.

Thank you to the OMS specialists who treat our OMS warriors, and a special thank you to NORD and Trio Health!
Audrey’s battle with OMS began in February 2010 when she was 7. She had just fought back-to-back bouts of strep throat when one morning her parents noticed her hand was shaking slightly. The next day she started waking up in the middle of the night in a screaming rage. She had a very hard time keeping her balance, even while sitting on a chair, and the rage fits became a daily event and her ability to focus was lost.

Her condition did not improve and her parents were getting frustrated as their household was in complete disarray. They did not know how to handle the rage attacks and Audrey’s loss of stability; to make matters worse, she also developed severe anxiety and OCD.

Audrey began a course of chemotherapy that lasted nearly 18 months. She also received regular IVIg treatments, speech and physical therapy, and took numerous medications to help her function with her special needs, such as Best Buddies, NH Special Olympics, and dance. She still struggles to manage it quite nicely.

Now, 8 years later, Audrey is a sophomore in high school and is very active in social programs involving others with special needs, such as Best Buddies, NH Special Olympics, unified sports, and dance. She still struggles at times with the effects of her OMS, but she manages it quite nicely.

Audrey got involved with OMSLife shortly after being diagnosed. She started a local teddy bear drive through OMSLife and a local charity called Annie’s Angels Memorial Fund. What started with 38 teddy bears is now more than 1500 teddy bears a year that Audrey gives to kids being treated at Boston Children’s Hospital. She has been recognized locally for her efforts in building the program to where it is today.
This began an almost 2-year journey of hope, joy, and despair. Braeden’s family treated his cancer at their hospital and traveled to an OMS specialist for confirmation and a treatment plan. The neurologist who miraculously knew just what he was seeing. He felt Braeden's abdomen, found his tumor, and explained what OMS and neuroblastomas are, and sent the family to Helen DeVos Children’s Hospital. Searching for answers led his parents to a pediatric neurologist who found his tumor and explained what OMS and neuroblastomas are, and sent the family to Helen DeVos Children’s Hospital. The changes were sudden and terrifying. Braeden underwent so much treatment and so many tests in an effort to treat his diseases. He had essentially been in the hospital and traveled to an OMS specialist for confirmation and a treatment plan. Braeden underwent so much treatment and so many tests in an effort to treat his diseases. He had essentially been in the hospital and traveled to an OMS specialist for confirmation and a treatment plan.

OMS treatment, which is usually continued for at least 1 to 2 years, should involve combined immunotherapies. While evidence is limited, the expert consensus for treatment involves a 3-agent protocol, with initial use of intravenous immunoglobulin (IVIg), rituximab, and either high-dose corticosteroids (IV methylprednisolone followed by pulse oral dexamethasone) or ACTH (corticotropin) appearing to have the best-documented outcomes for moderate and severe cases. Most children respond initially to treatment with high-dose steroids or ACTH, showing at least partial improvement. Those treated with steroids or ACTH alone, however, tend to promptly relapse when treatment is stopped. Over time, it is worth noting that treatment with corticosteroids or ACTH may have substantial cortisol-related adverse effects that should be monitored carefully, including weight gain, hypertension, and reduction in bone density. For OMS relapse, low-dose IV cyclophosphamide (3 to 6 cycles) or repeated courses of rituximab may have substantial cortisol-related adverse effects that should be monitored carefully, including weight gain, hypertension, and reduction in bone density. For OMS relapse, low-dose IV cyclophosphamide (3 to 6 cycles) or repeated courses of rituximab may be given. Oral weekly methotrexate may be a useful steroid-sparing agent in chronic relapsing-remitting disease.

Along with the above noted pharmacological agents, all children should receive appropriate physical, occupational, and speech therapy services. Formal neurodevelopmental and neurocognitive assessments should be performed over time to help develop individual educational accommodations.
Chloe, born a healthy baby girl in 1992, developed normally and met the child development milestones until the age of 5. After a fever and flu-like symptoms following her 18-month vaccination against MMR, her eyes became shaky when ill. She has some lasting side effects from long-term steroid use, but due to her determination and perseverance, Chloe is fully recovered from OMS. She has a great sense of humor, a positive outlook, and a strong personality. She continues to amaze and delight all who meet her and hear her story.

Investigational Therapies

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving US government funding, and some supported by private industry, are posted on this government web site.

For information about clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the NIH Patient Recruitment Office:

TTY: (866) 411-1010
Email: prpl@cc.nih.gov

For information about clinical trials sponsored by private sources, contact:

www.centerwatch.com

For information about clinical trials conducted in Europe, contact:

www.rarediseases.org

What is OMS?

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OUTCOME

Almost all children with neuroblastoma and OMS survive their tumor, which usually does not behave aggressively, though larger tumors may pose difficulties for resection. In contrast, the tumors associated with OMS in adults are often aggressive and can be fatal. The OMS relapse rate in children treated with only conventional agents is 50% to 75%. Increased immunosuppression has, however, improved neurodevelopmental outcomes in OMS. With more aggressive initial therapies in children, the relapse rate appears to be much lower. OMS onset in the first 2 years of life is particularly damaging to expressive speech and language development, and may result in a higher incidence of residual cognitive impairment. The best outcomes appear to be those involving early combination therapy and mild-to-moderate OMS severity. Failure to achieve complete neurological remission and multiple relapses may result in chronic-progressive OMS, with permanent deficits, such as attention deficit disorder (ADD), attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and irreversible cognitive impairment (low IQ). Children in the chronic state may become oppositional, depressed, or aggressive, and attention to these issues can help improve quality of life (QoL). Parents with a severely ill infant or child may develop “fragile child syndrome” and have difficulty ever seeing their child as a normal, thriving individual, with ‘ordinary’ behavioral issues of childhood misinterpreted to represent a relapse of OMS. These parents may benefit from counseling to gradually adjust the management of their child’s ongoing behavioral and developmental challenges.

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Meet OMS Warrior Cole

Cole

Cole was diagnosed with a medulloblastoma and OMS in July 2011, when he was 15 months old. His symptoms started with a viral infection and fever, and he went from a happy, playful toddler to an immobile baby in a few short days. He also started having brief intense, body tremors, speech, and eye movement abnormalities. He became very difficult to handle and was not necessarily crying but just extremely tense. He was not a happy baby; he was in pain and had a difficult time adapting to his surroundings.

Our goal as parents was to give our son the best possible chances to have a normal life, but we were quickly told that there was no known medical protocol for this condition, or research into this condition to follow. We were told that most children with OMS would have cognitive disabilities and behavioral issues. Our son and family would be facing a long and challenging road with long-term deficits and relapses. We were also told that OMS is a rare condition that did not have much funding or research. With the support of the staff and doctors and the efforts of our extended family, we decided to not give up our son and his battle. After many years, we saw some improvement, but it was not the same child we started with.

After many years of speech, occupational, and physical therapies, together with periods of isolation due to being immunocompromised, Cole is leading an amazing life. He is a public school in a regular class with no accommodations and is at level or even above level in some of his classes. He is loved by all who know him and has many friends. Cole is involved in many activities, such as Cub Scouts, golf, and basketball. He dreams of one day being an NFL football player. He is cautious and empathetic and puts others before himself. He doesn't look for the thrill of things. He prefers the things that are safe and comfortable. He doesn't ride roller coasters or go down tall water slides. He doesn't try new things to see if he will like them, but he enjoys them once he has decided he likes them. Sometimes we question if it is because of what he has gone through or if it is just who he is.

This has been a long journey with many up and downs and it has given us an old soul with a heart of gold. He is considerate and thoughtful and puts others before himself. We are so thankful for all the support that we have received. We are also very grateful for the amazing support we have received from the OMS community. We have been so blessed to have found a place where we are not alone and where we are accepted and loved. We are very thankful for all the support and encouragement we have received from others who have gone through the same things. We have also met many others who have gone through the same things and have decided to do all we can to make sure that they receive the same kind of support we have received. We have also met new friends and joined others who have gone through the same thing. Our experience has been a mixture of sadness and joy. We have shed many tears, we have also shed tears of happiness, happiness for watching our son do some of the simplest things. With the support of OMSLife over the years.

We thank the wonderful people at NORD and at Trio Health for the great opportunities they have provided to OMSLife. We appreciate the confidence you have in our organization.

For more information about the OMSLife Foundation, please go to our website at www.omslifefoundation.org or follow us on Facebook at www.facebook.com/OMSLifeinformation.
Meet OMS Warrior LAUREN

Lauren

In January 2009, our normally developing 26-month-old daughter began having difficulty balancing and within a couple days had stopped being able to sit and then lay down. She could no longer walk and was barely able to due to tremors and ataxia diagnostics had not led to a diagnosis. After 6 months of tests, no definitive diagnosis of pediatric neuroblastoma was made, and our daughter was given a 5-year survival rate. We continued to seek answers and support from various specialists. In May 2009, we were told she had elevated HVA/VMA catecholamine levels, possibly indicating neuroblastoma. We switched pediatricians at this time and continued to seek answers and support. Our second opinion led us to a diagnosis of OMS. OMS causes the body to attack itself, leading to multiple outcomes, including ataxia, tremors, eye movements, sleep disturbances, and rages/outbursts. She also had difficulty regulating her loudness at times (whether too loud or too soft), which indicated cerebellar involvement.

Her symptoms included ataxia, tremors, eye movements, sleep disturbances, and rages/outbursts. She also had difficulty regulating her loudness at times (whether too loud or too soft), which indicated cerebellar involvement. She began medication for seizures and 3 days of IV steroids to help with the cerebellar ataxia; her symptoms continued from page 21

In March 2012, she underwent an at-home surgery to hopefully bypass the complications she was having and went to 6.5 months post-ICP to a complication due to further complications. Lauren finally returned home in April 2012. As of 2013, she had fully recovered from the complications and surgery. Lauren continued her battle with OMS with the help of MyIg and CellCept®. This allowed her to make slow improvements in November 2014 and to gradually wean MyIg to 6 months after receiving it every 3 weeks for 6 years. Currently, we are trying to wean the MyIg to every 6 weeks and wean her off CellCept. Lauren is on her second port and her veins have not recovered from the excessive use when she was first diagnosed. Despite her OMS, Lauren is a well-adjusted child who excels remarkably in her studies and basketball. She is a graduate education student and was voted Class President. She is an above-grade level in academics and social and emotional development, and mostly struggles with fatigue and side effects after every MyIg treatment.

Lauren appears to be doing well but has made a huge leap in her ability to control her symptoms. Her progress has been slow, but we are happy to see improvements. We continue to seek answers and support from various specialists. In May 2009, we were told she had elevated HVA/VMA catecholamine levels, possibly indicating neuroblastoma. We switched pediatricians at this time and continued to seek answers and support. Our second opinion led us to a diagnosis of OMS. OMS causes the body to attack itself, leading to multiple outcomes, including ataxia, tremors, eye movements, sleep disturbances, and rages/outbursts. She also had difficulty regulating her loudness at times (whether too loud or too soft), which indicated cerebellar involvement. In March 2012, she underwent an at-home surgery to hopefully bypass the complications she was having and went to 6.5 months post-ICP to a complication due to further complications. Lauren finally returned home in April 2012. As of 2013, she had fully recovered from the complications and surgery. Lauren continued her battle with OMS with the help of MyIg and CellCept®. This allowed her to make slow improvements in November 2014 and to gradually wean MyIg to 6 months after receiving it every 3 weeks for 6 years. Currently, we are trying to wean the MyIg to every 6 weeks and wean her off CellCept. Lauren is on her second port and her veins have not recovered from the excessive use when she was first diagnosed. Despite her OMS, Lauren is a well-adjusted child who excels remarkably in her studies and basketball. She is a graduate education student and was voted Class President. She is an above-grade level in academics and social and emotional development, and mostly struggles with fatigue and side effects after every MyIg treatment.

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Long-term cognitive and physical issues are likely with delayed treatments and therapies. It is therefore highly recommended that physicians who are inexperienced in treating OMS coordinate the protocol with known specialists. Therapy is more effective with earlier treatments and therapies. The treatment protocol should be accompanied by non-pharmacological modalities, including:

- Speech therapy
- Occupational therapy
- Physical therapy
- Behavioral therapy

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Since OMS attacks the cerebellum of the pediatric patient during his or her formative years, prompt diagnosis of the disease and proper treatment is imperative to ensure the best outcome. While a new treating physician who has never seen a patient presenting these symptoms may easily misdiagnose the disease, the greater issue is when that physician chooses to take a “wait and see” approach in treatment of the disease.

Once accurately diagnosed, in almost all cases the treatment protocol outlined previously will present the best outcomes. Leading specialists in treating OMS across the United States agree this therapy produces the best results known at this time. Use of only one or two of these options, or administering all of them at sub-therapeutic doses, will typically deliver sub-optimal results.

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How you can help

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Michelle

Michelle’s journey with OMS began in 2010 when she was a 24-year-old graduate school student. Starting slowly, a flange in vertigo progressed over the following weeks to dizziness, difficulty walking, numbing, walking, and extremity and confusion, and converging muscle spasms. Despite months of ER visits, radiologists, and specialist visits, she did not receive a diagnosis. Michelle continued school but was clearly emotionally labile and socially withdrawn. She lived with her symptoms while she and her husband searched for an answer.

Throughout the following years she saw a handful of neurologists and had an array of tests, including MRIs, but the specialists could not find the cause of her symptoms. After months of ER visits and surgeries, Michelle had been diagnosed with OMS.

Michelle describes her OMS symptoms: "Making this diagnosis helps explain why I was suddenly, it began as vertigo but progressed over the following weeks to dancing eyes, full body shaking, nausea/vomiting, and extremely painful and contorting muscle spasms. Despite months of ER visits and procedures, she did not receive a diagnosis. Michelle continued school but was clearly emotionally labile and socially withdrawn. She lived with her symptoms while she and her husband searched for an answer.

During this time she continued to connect with other adults and parents of OMS warriors. Though she experienced occasional flares, she otherwise managed to function almost normally. She was able to continue her education and maintain her job as a research assistant in a laboratory. Michelle’s experience highlights the importance of continuing to advocate for awareness of OMS.

Michelle continued to receive IVIg treatment. Although she had great improvements with the IVIg, her symptoms slowly returned in the following months. During this time she continued to connect with other adults and parents of OMS warriors. Though she experienced occasional flares, she otherwise managed to function almost normally. She was able to continue her education and maintain her job as a research assistant in a laboratory. Michelle’s experience highlights the importance of continuing to advocate for awareness of OMS.

Michelle connected with an adult diagnosed with OMS who recommended she see the same provider. This adult had received a diagnosis of OMS and had noticed similar symptoms in her CSF, thus indicating an autoimmune component to her mysterious symptoms.

When she traveled from her home in Oregon to New York, the neurologist diagnosed her with OMS and recommended she receive IVIg treatment. Although she had great improvements with the IVIg, her symptoms slowly returned in the following months.

Thankfully, Michelle now lives a reasonably normal life with her family and dogs. She completed a doctorate degree and has maintained part-time work in the physiology research field. She also repairs web hosting and is a web developer.

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Meet OMS Warrior ZARA

Zara

Zara fought with OMS in May 2014 when she underwent a sudden change in her behavior, both physically and mentally. She lost her ability to sit and her emotionality that she had grown up to around 6 months old; she was active and responsive. Her behavior then turned agitated and she was found to have a neuroblastoma at Children’s Hospital (PCH) in search for a definite answer. December 2014 it could be a disorder called spasmus nutans, and Zara then had a neurological appointment at Phoenix Children’s Hospital where she was found to have opsoclonus/myoclonus syndrome (OMS).

Zara’s fight with OMS began in May 2014 when she underwent a sudden change in her behavior, both physically and mentally. She lost her ability to sit and her emotionality that she had grown up to around 6 months old; she was active and responsive. Her behavior then turned agitated and she was found to have a neuroblastoma at Children’s Hospital (PCH) in search for a definite answer. December 2014 it could be a disorder called spasmus nutans, and Zara then had a neurological appointment at Phoenix Children’s Hospital where she was found to have opsoclonus/myoclonus syndrome (OMS).

With symptoms such as ataxia and opsoclonus, Zara’s pediatrician thought it could be a disorder called spasmus nutans, and Zara then had a neurological appointment at Phoenix Children’s Hospital where she was found to have opsoclonus/myoclonus syndrome (OMS).

OMS in the REAL WORLD

Early and accurate diagnosis is important for these young patients because of potential detrimental effects of disease on neurodevelopment. Medications for treatment of OMS include IVIg, corticosteroids, ACTH, chemotherapies, and immunotherapies, and clinical data suggest that combination therapy of corticosteroids, ACTH, IVIg, and rituximab may be useful in preventing neurodevelopmental damage. In addition to medications, non-pharmacological therapies are typically prescribed to address speech, physical, occupational, and behavioral challenges. In many cases, treatment of OMS with the medications and therapies will typically take from 1 to 5 years to get the patient to baseline and in remission. During treatment or in the absence of disease control, medications to treat symptoms are commonly employed (e.g., sleep aids, proton pump inhibitors, mental health medications).

The outlook for patients with OMS is promising provided the continued trend of early diagnosis and early treatment. The main challenge to effective intervention is awareness, and the difficulty may be decreased through continued efforts of NORD, OMSLife, and publication of patient data from the OMS Natural History registry.

<table>
<thead>
<tr>
<th>Symptoms at Onset (n=150)</th>
<th>Per Cent</th>
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<tbody>
<tr>
<td>Ataxia</td>
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<td>40%</td>
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Percentage of Patients Using Therapy (n=117) Percentage of Benefit of Therapy Use

- Speech: 98% 98%
- Physical: 100% 100%
- Occupational: 98% 98%
- Psychological: 97% 97%
- Other: 48% 72%

Ancillary forms of therapy utilized by patients with OMS included oral medications, physical, and speech therapies, and psychological. These supplemental therapies are found to be beneficial by more than 90% of the patients who reported using them.

<table>
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<tr>
<th>Regimens by Start Date of IVIg (Start date of initial treatment for patients who did not take IVIg)</th>
<th>NO IVIg</th>
<th>IVIg+1 other medication</th>
<th>IVIg+2 other medications</th>
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<tbody>
<tr>
<td>NO IVIg</td>
<td>141</td>
<td>227</td>
<td>322</td>
</tr>
<tr>
<td>IVIg+1 other medication</td>
<td>21</td>
<td>72</td>
<td>80</td>
</tr>
<tr>
<td>IVIg+2 other medications</td>
<td>4</td>
<td>7</td>
<td>11</td>
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Initial Diagnosis Accuracy, Disease Severity, and Time from Onset to Diagnosis Over Time

- Accuracy of Diagnosis: 12%
- Disease Severity: 20%
- Time from Onset to Diagnosis: 10%

Table shows a decrease in incorrect initial diagnosis, disease severity, and time from onset to diagnosis.

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There are clusters of related symptoms that occur in OMS patients. These symptoms are present concurrently with opsoclonus/myoclonus syndrome, and tremors and ataxia are more prevalent when issues in sleep and opsoclonus/myoclonus are more frequent when tremors and opsoclonus/myoclonus are more frequent.

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