Quest

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EMPOWERING FAMILIES WITH INFORMATION AND INSPIRATION

MDA Muscular Dystrophy Association

SPECIAL EDITION:
2019 MDA CLINICAL & SCIENTIFIC CONFERENCE

PROGRESS IN MOTION

Delving into rapidly evolving science

NEW

zolgensma®
(onasemnogene abeparvovec-xioi)
suspension for intravenous infusion

Now Approved!

A one-time-only gene therapy for the treatment of children less than 2 years old with spinal muscular atrophy (SMA).

Indication and Important Safety Information

What is ZOLGENSMA?

ZOLGENSMA is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA). ZOLGENSMA is given as a one-time infusion into the vein. ZOLGENSMA was not evaluated in patients with advanced SMA.

What is the most important information I should know about ZOLGENSMA?

- Liver enzymes could become elevated and cause acute serious liver injury in children who receive ZOLGENSMA.
- Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function.
- Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, or if the patient misses a dose of the corticosteroid or vomits it up.

What should I watch for before and after infusion with ZOLGENSMA?

- Viral respiratory infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see signs of a possible viral respiratory infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.
- Decreased platelet counts could occur following infusion with ZOLGENSMA. Seek immediate medical attention if a patient experiences unexpected bleeding or bruising.

What do I need to know about vaccinations and ZOLGENSMA?

- Talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed to accommodate treatment with a corticosteroid.
- Protection against respiratory syncytial virus (RSV) is recommended.

Do I need to take precautions with the patient's bodily waste?

Temporarily, small amounts of ZOLGENSMA may be found in the patient's stool. Use good hand hygiene when coming into direct contact with bodily waste for 1 month after infusion with ZOLGENSMA. Disposable diapers should be sealed in disposable trash bags and thrown out with regular trash.

What are the possible or likely side effects of ZOLGENSMA?

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

The safety information provided here is not comprehensive. Talk to the patient's doctor about any side effects that bother the patient or that don't go away.

You are encouraged to report suspected side effects by contacting the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch, or AveXis at 833-828-3947.

Please see the Brief Summary of the Full Prescribing Information on the next page.

To learn more, talk to your doctor and visit ZOLGENSMA.com.

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avexis

IMPORTANT FACTS ABOUT ZOLGENSMA® (onasemnogene abeparvovec-xioi)

USE

ZOLGENSMA is a prescription gene therapy used to treat children less than 2 years old with spinal muscular atrophy (SMA).

- ZOLGENSMA is given as a one-time infusion into the vein.
- ZOLGENSMA was not evaluated in patients with advanced SMA.

WARNINGS

Acute Serious Liver Injury and Elevated Liver Enzymes

- Liver enzymes could become elevated and cause acute serious liver injury in children who receive ZOLGENSMA. Patients with pre-existing liver impairment may be at higher risk.
- Patients will receive an oral corticosteroid before and after infusion with ZOLGENSMA and will undergo regular blood tests to monitor liver function.
- Contact the patient's doctor immediately if the patient's skin and/or whites of the eyes appear yellowish, or if the patient misses a dose of the corticosteroid or vomits it up.

Decreased platelet counts could occur following infusion with ZOLGENSMA. Caregivers should seek immediate medical attention if a patient experiences unexpected bleeding or bruising.

OTHER IMPORTANT INFORMATION

Patients should be tested for the presence of anti-AAV9 antibodies prior to infusion with ZOLGENSMA.

Vaccination schedule should be adjusted where possible to accommodate treatment with an oral corticosteroid. Caregivers should talk with the patient's doctor to decide if adjustments to the vaccination schedule are needed during corticosteroid use. Protection against respiratory syncytial virus (RSV) is recommended.

Viral respiratory infections before or after ZOLGENSMA infusion can lead to more serious complications. Contact the patient's doctor immediately if you see signs of a possible viral respiratory infection such as coughing, wheezing, sneezing, runny nose, sore throat, or fever.

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COMMON SIDE EFFECTS

The most common side effects that occurred in patients treated with ZOLGENSMA were elevated liver enzymes and vomiting.

These are not all the possible side effects. Talk to the patient's doctor about any side effects that bother the patient or that don't go away.

QUESTIONS?

To learn more, talk to your doctor and you can visit www.ZOLGENSMA.com for Full Prescribing Information.

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Bannockburn, IL 60015

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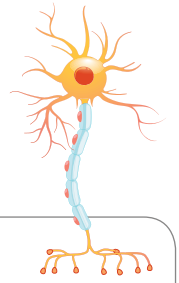
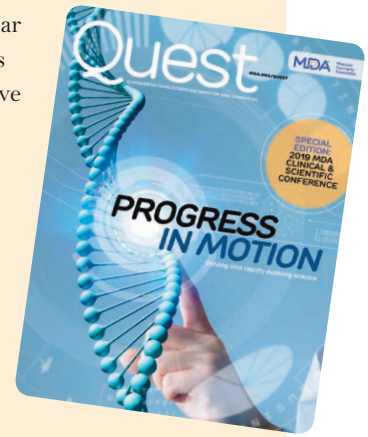


MORE ONLINE

In a panel discussion, FDA directors and neurology professors weighed in on developing new drugs for neuromuscular diseases. Read exclusive coverage of the informative conversation online at mda.org/quest.

Introducing *Quest* Clinical & Scientific Conference Edition

Historically, MDA has hosted two industry conferences, one for clinicians to discuss new care paradigms and one for researchers to discuss the latest in neuromuscular disease science, held in alternating years. But with more neuromuscular disease treatments and trials in play than ever before, we've begun a new conversation.



This year, MDA combined its conferences for the first-ever Clinical & Scientific Conference in Orlando, Fla. Themed "Progress in Motion," the conference facilitated interdisciplinary collaboration among clinicians, scientists, policymakers, and nonprofit and industry leaders.

In this special issue of *Quest*, you'll read about conference sessions that illustrate common lessons across different disease states and delve into rapidly evolving topics. Find more conference coverage at **mda.org/quest**.

2019 MDA CLINICAL & SCIENTIFIC CONFERENCE STATS

1,200+ researchers, clinicians, industry and pharma partners in attendance

23 research-focused sessions

136 oral presentations on ongoing work

300+ posters detailing current research

Opening Statements

MDA's president and chairman of the board kicked off the conference

After welcoming attendees to the 2019 Clinical & Scientific Conference, MDA President and CEO Lynn O'Connor Vos put the moment in perspective.

"If we reflect for a moment on where we were as a community five years ago, we are making great progress," she said. "Disease-modifying therapies are no longer a thing of the future, and we are at the forefront of new treatment paradigms. We are all united by the urgent need to bring innovative care, cutting-edge clinical research and new breakthrough treatments to our community."

Lynn O'Connor Vos

The conference opened on April 15, which was International Pompe Day. MDA Chairman of the Board R. Rodney Howell, M.D., added further context with a personal story about meeting the family of Joannes Cassianus Pompe, the pathologist who first characterized the disease in 1932. Thanks to Pompe's work, when the age of newborn screening began, babies with the disease could be identified and treated.

"We're screening populations now for spinal muscular atrophy and Pompe," Dr. Howell said. "With any luck we will soon be starting newborn screening for Duchenne muscular dystrophy." (See "The Case for Newborn Screening" on page 10.)

Meet the MDA National Ambassadors

Three people are serving in this important role

MDA's 2019 National Ambassadors from left to right: Justin Moy, Tana Zwart and Faith Fortenberry.

MDA's three National Ambassadors — including Tana Zwart, named an ambassador in 2019 — spoke during the conference's opening ceremony. They shared their experiences as ambassadors and as people living with neuromuscular diseases.

Zwart, a 34-year-old Sioux Falls, S.D., resident who lives with fascioscalpulohumeral muscular dystrophy (FSHD), has been involved with MDA since her diagnosis at age 7. She appeared in local MDA telethons, organized high school fundraisers and now helps plan MDA gala events in Sioux Falls. The organization has been part of the strong support system she spoke about at the conference.

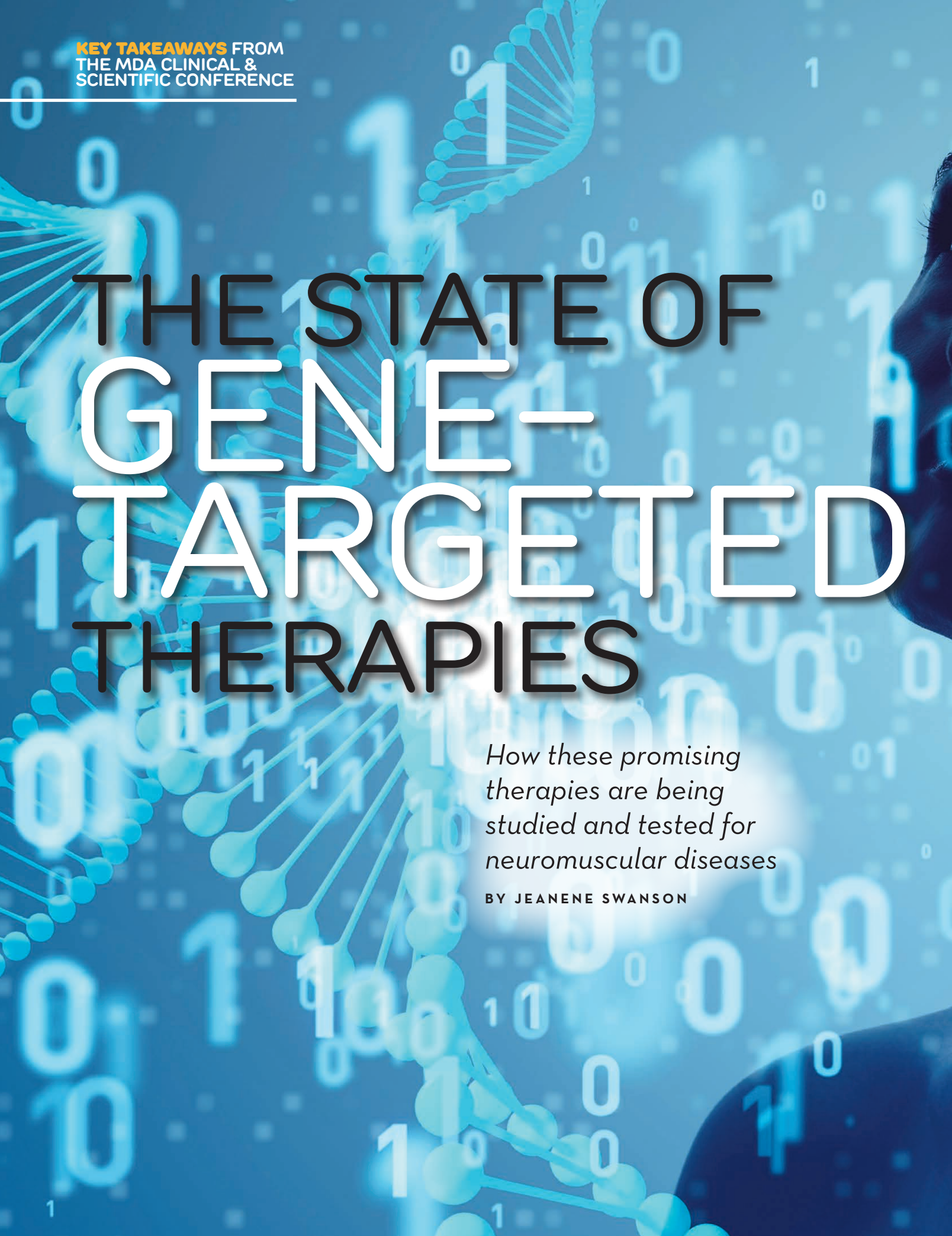
"I've always had a very tremendous support system in my friends and family and even my community," she said. "They've always believed in everything I did and helped me get through things. My position definitely has always been 'I can figure that out, I can make that work.' … Quitting is not really in my vocabulary."

It's not in National Ambassador Faith Fortenberry's vocabulary, either. The 7-year-old from Waco, Texas, lives with spinal muscular atrophy (SMA) and, thanks to treatment with Spinraza, has been able to stop breathing treatments and bilevel positive airway pressure (BiPAP) use overnight. With more respiratory strength and stamina, Faith is doing big things, like starring in the lead role in a local production of "Annie."

An appreciation for innovation colored National Ambassador Justin Moy's remarks. The 18-year-old Concord, Mass., native, who lives with congenital muscular dystrophy (CMD), spoke in the midst of his freshman year at Worcester Polytechnic Institute in Massachusetts, where he is studying bioinformatics.

"As I'm sure a lot of you are aware, biology and the sciences aren't the easiest things in college, but I've definitely had a lot of fun getting to learn what you all know," he told the audience of clinicians and researchers. "I want to be able to contribute to the fight against neuromuscular disease."

All three MDA National Ambassadors surely have bright futures and an exciting year ahead of them.



THE STATE OF GENE-TARGETED THERAPIES

How these promising therapies are being studied and tested for neuromuscular diseases

BY JEANENE SWANSON

The first full day of MDA's Clinical & Scientific Conference included a highly anticipated session that took a deep dive into gene-targeted therapies. Experts discussed how gene-replacement, gene-silencing and gene-editing therapies are being studied and tested for treating patients with a variety of neuromuscular diseases (NMDs).

In "Ongoing Clinical Trials" on page 7, we share progress from some of the most promising clinical trials for NMDs such as Duchenne muscular dystrophy (DMD), facioscapulohumeral muscular dystrophy (FSHD) and spinal muscular atrophy (SMA). Many of these studies are testing gene-targeted therapies that focus on the genetic, or root, cause of the disease. If approved, these new therapies will play a large role in advancing the field of genetic medicine — not only as it pertains to NMDs, but for all diseases with a known genetic basis.

GENE REPLACEMENT IN DMD

Jeffrey Chamberlain, Ph.D., a researcher at the University of Washington School of Medicine, discussed the development of gene-replacement therapies for DMD using micro-dystrophin, a miniaturized version of the dystrophin gene. The underlying cause of DMD is an absence or deficiency of the muscle protein dystrophin due to a mutation in the *DMD* gene, and micro-dystrophin can produce a functional protein to substitute for the missing dystrophin. Dr. Chamberlain has been working for 30 years on optimizing micro-dystrophin design to improve localization and functionality.

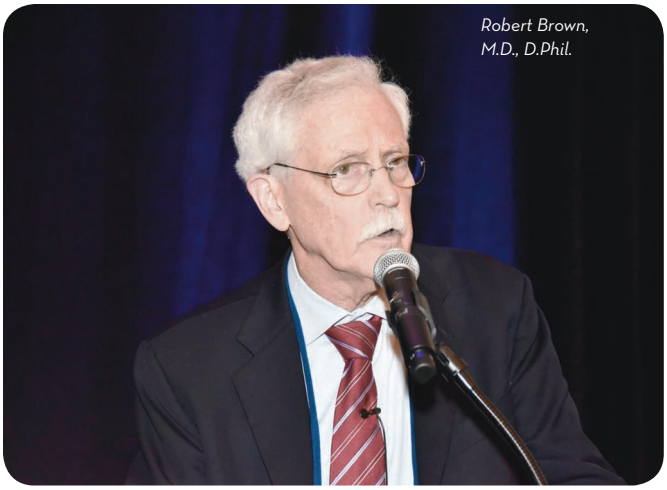
In preclinical animal studies, Dr. Chamberlain demonstrated that treatment with an adeno-associated virus (AAV) vector carrying a micro-dystrophin gene resulted in significant improvement in muscle morphology and strength. (In gene-replacement therapy, AAVs are used to deliver a normal copy of a missing or mutated gene to a patient's cells.) He also presented data showing that expression of this micro-dystrophin in animal muscle is stable for more than two years and is appropriately localized within the cell. Dr. Chamberlain's experimental gene therapies have been licensed to Solid Biosciences for clinical development. Solid is currently conducting a phase 1/2 clinical trial, called IGNITE DMD. (Flip this issue and turn to page 8 of "Progress Now" to learn more.)

Barry Byrne, M.D., Ph.D., director of the Powell Gene Therapy Center at the University of Florida and the principal investigator on IGNITE DMD, presented interim results from the clinical trial. The IGNITE DMD trial is designed to test up to three doses of the AAV vector carrying micro-dystrophin for safety and efficacy in boys with DMD. The study has enrolled six patients thus far, three to the first cohort and three to the delayed-treatment cohort. The first three patients received the lowest planned dose. As reported in February, initial muscle biopsies after three months showed low levels of micro-dystrophin protein expression. Based on these results, the company is planning to increase the dose in the next cohort as soon as possible.

GENE SILENCING IN ALS

Robert Brown, M.D., D.Phil., a researcher at the University of Massachusetts Medical School and a pioneer in the field of ALS whose team discovered the first gene linked to the inherited form of the disease, talked about progress in using gene silencing to treat ALS.

"The disease, as we all know, is one of the worst in neuromuscular clinical experience," he said, so getting therapies to the clinic as soon as possible is a priority. About 10% of ALS cases arise because of inherited genetic



Robert Brown, M.D., D.Phil.

Dr. Brown believes that gene silencing has proven feasible for at least two ALS genes (SOD1 and C9ORF72) using multiple approaches.

defects, and it is thought that mutations in the superoxide dismutase 1 gene (*SOD1*) cause a subtype of familial ALS that makes up 2% of all ALS cases. In addition to *SOD1*, the *C9ORF72*, *TDP-43* and *FUS* genes are other therapeutic targets that have been linked to causing ALS, bringing the confirmed ALS gene total to more than 40.

Both researchers and companies, including Biogen, Wave Life Sciences and AveXis, are developing approaches to silence toxic genes in ALS. In research published in 2018, Dr. Brown showed that *SOD1* could be silenced in non-human primates. Based off this work, he recently tested this approach in a compassionate-use study on an ALS patient. At two months after treatment, the 22-year-old patient still showed disease progression. However, the patient's SOD1 protein levels in cerebral spinal fluid were reduced by 14%.

"That is a lot — a 50% decrease almost cures ALS," Dr. Brown said. "It doesn't take too much silencing to get some kind of benefit."

Dr. Brown believes that gene silencing has proven feasible for at least two ALS genes (*SOD1* and *C9ORF72*) using multiple approaches. These strategies are likely to be tested with other toxic ALS genes, and the data support the view that early intervention is critical.

GENE-EDITING THERAPIES

Another type of gene-targeted therapy is gene editing. In gene editing, a permanent change is made in a faulty gene, thereby fixing the underlying genetic cause of a disease. Several of the talks at the conference focused on using CRISPR-Cas9 (also called CRISPR) to correct genes for DMD, FSHD, Becker muscular dystrophy (BMD) and myotonic dystrophy (DM).

Charles Gersbach, Ph.D., a researcher at Duke University, discussed experiments in an animal model of DMD using an AAV vector to deliver the CRISPR platform. He summarized the state of the field:

"Genome editing for DMD typically focuses on removing gene segments to restore functional, truncated dystrophin," he said, underscoring that, "CRISPR-based genome editing restores long-term dystrophin expression in many animal studies with no reported adverse effects."

However, there are still outstanding safety concerns, including that people could have an immune response to CRISPR or that it could cause non-specific changes in a person's genome. "Additional research is required to understand implications of the immune response, long-term presence of CRISPR and non-specific genome modifications," Dr. Gersbach said.

Melissa Spencer, Ph.D., a researcher at the University of California, Los Angeles, spoke about using nanoparticles as an alternative method to AAVs to deliver CRISPR for treating DMD. Nanoparticles have many benefits compared to AAVs, including that they are easier to manufacture and have the potential to be administered more than once.

Dr. Spencer's CRISPR therapy will target the "hotspot" where the majority of mutations occur within the *DMD* gene. In preclinical studies she found that her nanoparticle-delivered CRISPR therapy, which is designed to restore a functional dystrophin gene in up to 50% of patients, is effective in cultured cells and in a mouse model. Her lab is further optimizing the nanoparticles for efficiency.

AAVS AND IMMUNE RESPONSE

Manuela Corti, P.T., Ph.D., a researcher at the University of Florida, discussed the importance of immune modulation in AAV-mediated gene delivery because the immune response is a universal problem when using AAVs. She is continuing to test the hypothesis that immunosuppression by depleting B cells (a type of immune cell) prior to administering AAVs would block immune responses to the vector, thereby allowing for repeat administration and increasing efficacy. Q

Jeanene Swanson is MDA's healthcare content and public relations manager.

Gene-Targeted Therapy Explained

From CRISPR to vectors, the topic of gene-targeted therapy can be confounding. Flip this issue and turn to page 16 for a primer on gene-targeted therapies and definitions of common terms.

ONGOING CLINICAL TRIALS

Updates on some of the most promising studies

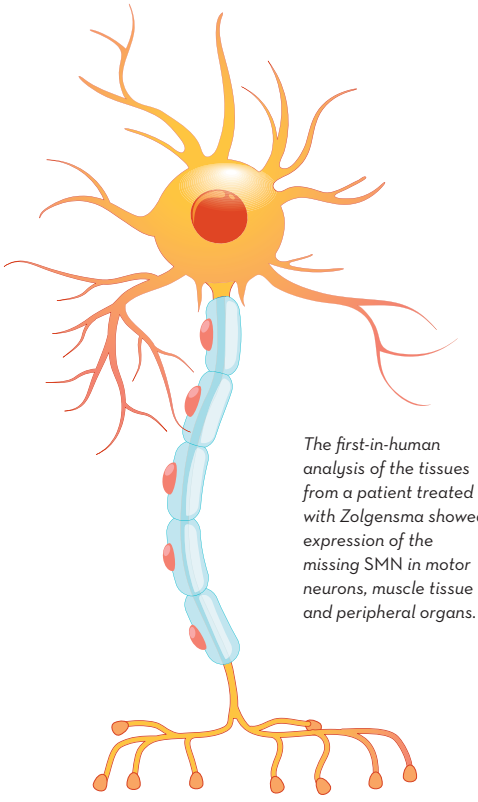
BY ORI ROKACH, Ph.D.

During the second day of the 2019 MDA Clinical & Scientific Conference, 14 scientists and clinicians shared exciting updates from the pipeline of clinical trials. Below are highlights from the session.

ZOLGENSMA FOR PATIENTS WITH SMA

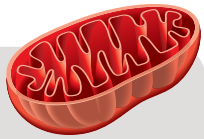
At the time of the conference, Zolgensma (onasemnogene abeparvovec-xioi, or AVXS-101) was under review by the U.S. Food and Drug Administration (FDA). In May, the FDA approved the drug as a therapy for the treatment of children younger than age 2 with spinal muscular atrophy (SMA).

At the conference, Brian Kaspar, Ph.D., chief scientific officer of AveXis, presented clinical trial results of Zolgensma, a single-administration gene-replacement therapy. The treatment delivers the *SMN* gene to targeted motor neurons and other tissues using a viral vector called adeno-associated virus 9 (AAV9) for patients with SMA. This is a severe neuromuscular disorder caused by a genetic defect in the *SMN1* gene. Individuals with SMA experience loss of motor neurons and progressive muscle weakness, leading to paralysis. Analysis showed that Zolgensma successfully crosses the blood-brain



The first-in-human analysis of the tissues from a patient treated with Zolgensma showed expression of the missing SMN in motor neurons, muscle tissue and peripheral organs.

TRIAL TERMINOLOGY



Blood-brain barrier: The highly selective border that tightly regulates the passage of molecules from blood circulating through the body into the central nervous system.

Central nervous system: The part of the nervous system that consists of the brain and the spinal cord.

Mitochondria: This powerhouse of the cell is responsible for energy production, permitting metabolism and routine cellular function.

Pharmacological chaperone: A small molecule that properly folds and stabilizes a protein.

Flip this issue and turn to page 20 to learn more common research terms.

barrier to target the central nervous system in humans. The first-in-human analysis of the tissues from a patient treated with Zolgensma showed expression of the missing *SMN* in motor neurons, muscle tissue and peripheral organs.

Dr. Kaspar also provided an update on an ongoing phase 3 trial in which Zolgensma is being tested in patients with SMA type 1. Zolgensma treatment was associated with prolonged survival, an increase in motor function and achievement of motor milestones inconsistent with the normal course of SMA type 1 disease progression. Zolgensma is currently being tested in phase 3 trials for SMA type 1 and pre-symptomatic SMA and is in phase 1 for SMA type 2.

ACE-083 FOR PATIENTS WITH FSHD

Jeffrey Statland, M.D., of the University of Kansas Medical Center, presented Acceleron Pharma's results on its phase 2 trial of ACE-083 in both healthy individuals and people living with facioscapulohumeral muscular dystrophy (FSHD). The FDA has granted ACE-083 Fast Track and Orphan Drug designations for FSHD and Charcot-Marie-Tooth disease (CMT). FSHD is a genetic muscle disorder in which the muscles of the face, shoulder blades, upper arms and lower legs are among the most affected. ACE-083 is designed to increase the strength and the function of the muscles most affected in patients with FSHD by inhibiting selected proteins in the TGFβ superfamily that are responsible for reducing muscle growth, such as myostatin and activins.

ACE-083 was found to be well tolerated after local injection in the tibialis anterior (TA) or biceps brachii (BB) muscles, and over a period of three months in patients diagnosed with FSHD. A dose-dependent increase in the total muscle volume was observed: a greater than 15% increase in the total muscle volume was measured in patients treated with 200 mg or 240 mg, and fat fraction decreased in the TA, which suggests improved muscle quality. Currently, the placebo-controlled part 2 of this phase 2 study is ongoing.

Jeffrey Statland, M.D.

SUVODIRSEN FOR PATIENTS WITH DMD

Kathryn Wagner, M.D., Ph.D., director of the Center for Genetic Muscle Disorders at the Kennedy Krieger Institute, presented Wave Life Sciences' results of a successful first-in-human trial that supports the initiation of a phase 2/3 efficacy and safety trial (DYSTANCE 51) of suvodirsen (WVE-210201) in patients with Duchenne muscular dystrophy (DMD) amenable to exon 51 skipping. DMD is a genetic disorder characterized by progressive muscle degeneration and weakness due to loss of dystrophin, a protein that helps keep muscle cells intact. Suvodirsen is an antisense molecule that allows the cellular machinery to "ignore" the mutation and continue to produce full-length

Kathryn Wagner, M.D., Ph.D.

dystrophin. Suvodirsen was generally safe and tolerable up to a dose of 5mg/kg.

ATB200/AT2221 FOR PATIENTS WITH POMPE DISEASE

Tahseen Mozaffar, M.D., director of the MDA ALS Neuromuscular Center at the University of California, Irvine, presented clinical trial results of Amicus Therapeutics's ATB200/AT2221 in adults with Pompe disease. Pompe patients have a deficiency in active acid alpha-glucosidase (GAA) enzyme, and as a result, glycogen accumulates in their skeletal and heart muscle tissue. ATB200 is a recombinant human GAA enzyme that was developed to replace the faulty GAA enzyme. This is called enzyme-replacement therapy (ERT).

In this trial, ATB200 was paired with AT2221, a pharmacological chaperone that protects ATB200 while it is in the bloodstream so more active enzymes can be delivered to the muscle tissue. Data from this interim analysis showed functional benefits of ATB200/AT2221; trial participants' six-minute test results, muscle strength and daily living activities were improved. Pulmonary function was improved in patients who were never introduced to ERT before, and creatine kinase (CK) was reduced. ATB200/AT2221 was tolerated over more than 30 months of treatment.

DEOXYNUCLEOSIDE THERAPY FOR PATIENTS WITH TK2-RELATED MITOCHONDRIAL DNA DEPLETION

Michio Hirano, M.D., of the Columbia University Medical Center, presented clinical trial results of Modis Therapeutics' promising therapy for patients diagnosed with TK2-related mitochondrial DNA depletion syndrome. Thymidine kinase 2 (TK2) is required for the synthesis of mitochondrial DNA, and individuals deficient in TK2 have reduced mitochondrial DNA and a resulting myopathy. Dr. Hirano developed a treatment strategy by which the building blocks of mitochondrial DNA are given in an attempt to overcome the deficit.

Results from an expanded-access, compassionate-use program led by Dr. Hirano showed that six-minute walk tests improved in 8 out of 9 patients (89%), including one patient who regained independent ambulation. Four out of 5 patients were able to discontinue with their feeding tubes. Two out of 10 patients who required mechanical ventilation were able to breathe independently. Moreover, five patients who were diagnosed with early onset and severe disease improved their survival and motor functions significantly compared to historically untreated patients. Q

Ori Rokach, Ph.D., is a biomedical writer for MDA.

Michio Hirano, M.D.

Keep Up With Research

Flip this issue and turn to page 6 to read "Progress Now," our guide to research updates and breakthroughs.

THE CASE FOR NEWBORN SCREENING

Identifying neuromuscular diseases at birth can yield great benefits but faces great challenges

BY CHRISTOPHER ANSELMO

Newborn screening allows babies born with life-threatening diseases to be treated before they show any signs of disease, which can lead to improved outcomes and maybe even a life free of symptoms.

As therapies for neuromuscular diseases progress through the clinical pipeline and get approved by the U.S. Food and Drug Administration (FDA), the importance of newborn screening is heightened. Currently, it is recommended that states screen for Pompe disease and spinal muscular atrophy (SMA), and a screening for Duchenne muscular dystrophy (DMD) could be on the horizon. But despite these advancements, some states face implementation challenges due to scientific, economic and operational considerations. This was the focus of the newborn screening session at the MDA Clinical & Scientific Conference.

WHY DOES NEWBORN SCREENING MATTER?

"Time is motor neuron," said Richard Finkel, M.D., a pediatric neurologist at Nemours Children's Health System in Orlando, Fla., and a presenter during the session. Even for children who are diagnosed with SMA types 3 and 4 (milder forms of the disease), any delay in treatment can have significant impact down the line. "Why wait for children to become symptomatic?" Dr. Finkel asked. "Children cannot reclaim lost motor neurons."

Newborn screening can provide the earliest possible diagnosis and intervention for life-threatening conditions. It's critically important because, in many cases of progressive, degenerative diseases, what is lost cannot be regained.

THE STATES OF SCREENING

The Recommended Uniform Screening Panel (RUSP) is a list of disorders for which the U.S. Department of Health and Human Services (HHS) recommends states screen. However, HHS does not mandate states' screening policies. Presenters at the conference provided insight into the RUSP standings for neuromuscular disease screenings.

Barry Byrne, M.D., Ph.D., director of the Powell Gene Therapy Center at the University of Florida, updated the audience on the implementation of newborn screening for Pompe disease, which has had an FDA-approved therapy, Sanofi-Genzyme's Lumizyme, on the market for several years. Pompe was added to the RUSP in 2015, and the screening has been gradually adopted by states throughout the country. Dr. Finkel discussed the recent success of SMA's addition to the RUSP, explaining that 17 states currently are in some phase of SMA screening.

Yet according to the speakers, even with both conditions officially on the RUSP, state-by-state adoption is hampered by challenges that include legislative delays and funding issues.

Peter Kang, M.D., a pediatric neurologist at the University of Florida, addressed current efforts to add DMD to the RUSP. Even though meaningful treatments for DMD are progressing through clinical development, it will be challenging to add the disease to the RUSP. Success faces issues such as the proven efficacy of DMD therapies and the accuracy of diagnosing newborn DMD patients.

However, learnings from the processes of adding Pompe and SMA to the RUSP can inform ways to make a case for adding DMD.

ADVOCACY'S ROLE

The final discussion of the day centered on the role advocacy plays in educating lawmakers about the importance of newborn screening. Maintaining current funding levels for research and the implementation of newborn screening, on both the federal and state levels, still requires a lot of legwork. Additionally, the treatment field is moving quickly as researchers gain a better understanding of disease progression, disease-causing genes and new therapies.

Yet the need is real: We must screen for diseases so that one day, more babies can have access to lifesaving treatments.

John Crowley, CEO of Amicus Therapeutics and father of two children living with Pompe disease, emphasized this point at the conclusion of the panel. "It would be a tragedy to have all these new therapies available and [be] years behind in finding the children," he said. "We should be years ahead." Q

Christopher Anselmo is a market intelligence manager for MDA.

HOW IS A CONDITION ADDED TO STATE SCREENING PANELS?

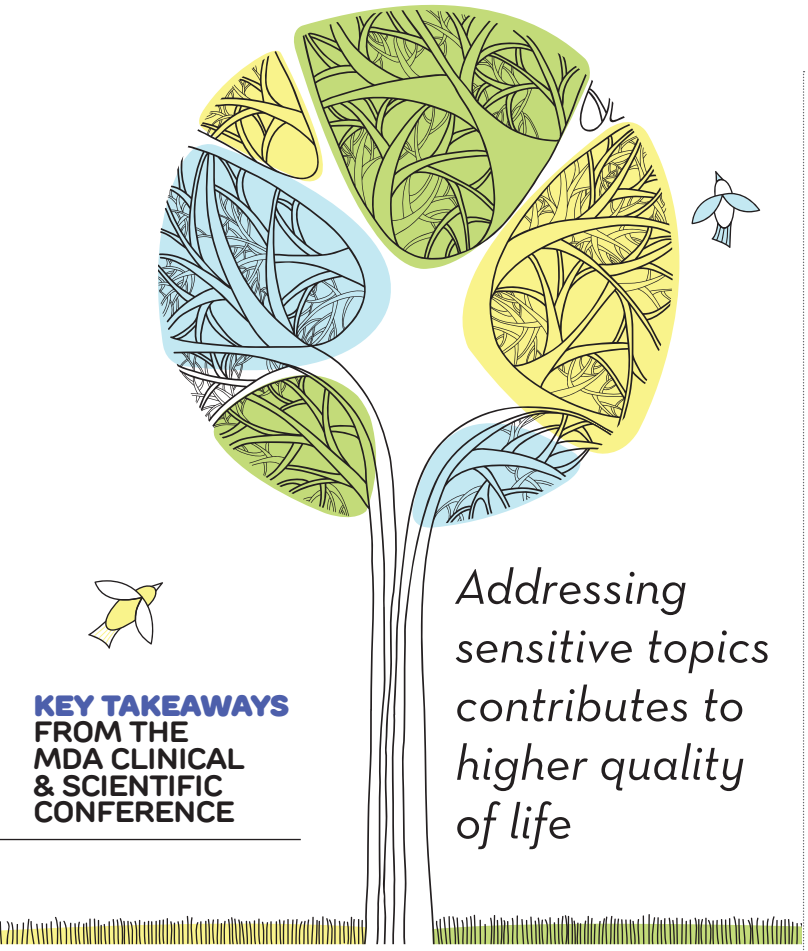
Three criteria must be met before a disease can be added to a newborn screening panel:

1. Evidence must support a benefit to screen for the condition in newborns.
2. States must have scientific and financial feasibility to screen for the condition.
3. An FDA-approved therapy that can treat the condition must be available.

If those criteria are met, a federal advisory committee composed of clinicians, researchers, public health experts, patient advocates, disease experts and newborn screening leaders reviews all available information and makes a formal recommendation to the Secretary of Health and Human Services. From there, the secretary may add it to the Recommended Uniform Screening Panel (RUSP).

The RUSP, although influential, is non-binding on states. Each state's public health department decides whether to include the disease on their newborn screening panel, taking into consideration the cost to taxpayers and state public health laboratory and physician capacity.

To find conditions screened in each state, visit **babysfirsttest.org/newborn-screening/states**.



KEY TAKEAWAYS FROM THE MDA CLINICAL & SCIENTIFIC CONFERENCE

Addressing sensitive topics contributes to higher quality of life

CARE ACROSS THE LIFESPAN

BY LUCJA GRAJKOWSKA, Ph.D.

The patient journey starts with a diagnosis and often involves pediatric-to-adult transition, clinical follow-ups and multidisciplinary disease management. In recent years, the care model for neuromuscular disease has evolved into a patient-centric treatment approach, in which individuals are driving their own care decisions.

This approach was the focus of the Care Across the Lifespan session at MDA's Clinical & Scientific Conference. The session revealed that many people with neuromuscular disease are living longer lives with higher quality of life, in particular because of improvements in the diagnostic process, a robust drug development pipeline with increased clinical trial opportunities, the increased availability of multidisciplinary MDA Care Centers and improved management of disease symptoms.

The incorporation of professionals with experience in nutritional, respiratory, psychosocial and mobility aspects of neuromuscular illness means that many everyday problems can be addressed. As part of this, patients are better able to have difficult but important conversations with their providers — specifically with respect to sexual health and end-of-life care.

TALK ABOUT SEX

Sarah Stoney, M.S.W., L.S.W., a licensed clinical social worker at Children's Hospital of Philadelphia, spoke about an underdiscussed topic: sexual health for inidividuals with neuromuscular disease. She addressed issues surrounding body image, challenges in advocating for sexual health, and ways patients and care teams can normalize these conversations.

Young adults with progressive illnesses often have a complex relationship with their body image that is compounded by a lack of representation in the media. Many patients report feeling they may not be able to have sex; are weak, asexual or infertile; that they may not ever fit the role of spouse or parent; or that their medical needs outweigh their sexual needs.

Family planning is also an underdiscussed topic for women with neuromuscular disease. Pregnancy and childbirth with these conditions can be more complex, and many women find themselves underprepared because of a lack of information.

Individuals with physical disabilities and neuromuscular disease are entitled to a positive sexual identity, Stoney asserted. She encouraged the care teams of individuals with neuromuscular diseases to acknowledge and validate the importance of healthy sexuality. Sometimes, the best resource is a peer group that can offer information and support.

PLAN AHEAD

Often, when patients are referred to hospice care, they haven't been asked about their preferences. Members of the care team tend to delay the conversation because they don't want to take away hope or contribute to feelings of depression. However, as Nancy Glass, M.D., M.B.A., of Texas Children's Hospital, discussed at the conference, failure to plan can create more distress, not less.

Dr. Glass emphasized that individuals with progressively degenerative diseases are aware of their decline and likely have end-of-life issues on their minds already — so clinicians need to talk about it. Discussing advance directives, do-not-resuscitate orders and hospice plans actually puts patients in control and helps identify those who can make decisions.

A vital piece of the discussion is providing accurate information about the patient's options. There is an important difference between palliative care and

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Care Across the Lifespan panelists, from left to right: Nancy Glass, M.D., M.B.A., F.A.A.P.; Catherine Lomen-Hoerth, M.D., Ph.D.; James Wymer, M.D., Ph.D.; Sarah Stoney, M.S.W., L.S.W.; John Brandsema, M.D.; Diane Murrell, L.C.S.W.

hospice care. Palliative care is part of the treatment plan and should be discussed early on to help decide the goals of care, irrespective of the prognosis. Hospice care is for patients who are reasonably expected to live no longer than six months. Recent legislation has ensured that Medicaid patients in hospice care are able to receive active therapy, which means there is no reason to delay a referral to hospice. An earlier referral allows the hospice team to form a relationship with the patient and provide support.

A conversation about the goals of care is essential to ensure the best quality of life for a patient. This conversation should take place in a calm setting, not during a health crisis. If a patient does experience a health crisis, previously discussed goals can guide the care team in its decisions.

PARTING THOUGHT

Difficult and uncomfortable conversations are essential in advancing the patient-centered care model. Care teams should approach these conversations with the idea that all patients are entitled to the dignity of the full human experience — and patients deserve the opportunity to access information and address these areas. Q

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