



## FDA Listening Session on Inclusion Body Myositis March 5, 2020



FDA held a Listening Session with Inclusion Body Myositis (IBM) patients and care partners on March 5, 2020. Patient Listening Sessions are intended to be a resource for the FDA's medical product centers to engage with patients and their advocates. The IBM session was patient-led, meaning that The Myositis Association (TMA) requested and received the opportunity to share its members' perspectives with the FDA.

## **The meeting followed the following agenda.**

### **I. FDA Welcome**

A. Andrea Furia-Helms, Director of FDA's Patient Affairs Staff opened the meeting on behalf of the FDA by welcoming TMA and thanking the speakers for their participation in the session. She highlighted the Agency's interest in conducting meetings such as this one to hear directly from patients to help the FDA representatives understand the symptoms and disease burden of IBM and to use that information to inform medical product development (MPD).

B. Susan Chittooran, Patient Engagement Project Manager, added her welcome and explained the procedures that would be followed during the meeting. Of particular interest, she let the participants know that should there be any unanswered questions following the meeting, that Patient Affairs would be happy to seek out and provide answers from FDA.

### **II. The Myositis Association's Presentations**

A. Mary McGowan, Executive Director of TMA, thanked the FDA for the opportunity to meet and introduced TMA as the leading organization that exists to support researchers, patients and care partners in the search for treatments for IBM. She spoke of some of the key struggles faced by persons with IBM and their care partners on a daily basis, highlighting the debilitating and life altering impacts of the disease. She described the urgency felt by everyone associated with the disease, and outlined TMA's history in providing \$7 million in research grants that have advanced scientific knowledge via collaborations with medical institutions and organizations such as International Myositis Assessment & Clinical Studies Group (IMACS) and the National Organization for Rare Disorders (NORD).

B. Eight patients and care partners then spoke about their daily lives and the burden and experience of living with IBM.

C. Dr. Tom Lloyd, Chair of the Research Committee of TMA's Medical Advisory Board spoke about his experience treating patients with IBM and being a clinical researcher.

### **III. Dialogue and a Q&A period followed the presentations**

## **Summary of topics discussed**

**IBM Patients and care partners consistently described their experience with a common set of debilitating symptoms that significantly impacted their daily lives. The symptoms themselves, and the description of the severity, varied somewhat between speakers but taken together, provided a comprehensive description of the burden of disease along the continuum of disease progression.**

1. The hallmark symptom of IBM is muscle weakness and atrophy, followed by loss of muscle function. IBM is relentlessly progressive and eventually results in near total disability.
2. All speakers described muscle weakness that has progressed over a period of years, with the initial effects on the quadriceps and hip flexors and/or the finger flexors.
  - a. Lower limb impacts lead to loss of mobility, as getting up from a chair, walking, and climbing steps becomes increasingly difficult and eventually impossible. Falls are frequent. As the disease progresses, transfers require assistance from a care partners and eventually from lift equipment such as ceiling or Hoyer lifts.
  - b. Upper limb weakness leads to reduced grip strength and manual dexterity, significantly impacting activities of daily living such as writing, typing, toileting, dressing, eating, preparing food, and carrying items.

- c. Some patients described their experience with dysphagia, which affects over half of IBM patients and can lead to choking and aspiration pneumonia. One patient's struggle with excessive phlegm was detailed.
  - d. Other patients described fatigue associated with extra effort required to compensate for their physical weakness and disabilities.
3. Care partners provided their perspective on the increased need for support and caregiving to assist patients with activities of daily living as their disease progresses. Several late stage patients are almost completely quadriplegic. Providing care can become the equivalent of a fulltime job for spouses, family members and aides.
  4. Patients/care partners indicated that they often experience depression related to their condition, and due to limited mobility, the logistics associated with going out are daunting. Social isolation is common and a major concern.

**IBM patients and care partners described a number of impacts and concerns that go beyond the physical symptoms and functional losses.**

1. Most patients and care partners struggle with the uncertainty about the future. While all know that progression is inevitable, the timing is uncertain making planning for the future very difficult. Several noted that their lives were very different from the active retirement they had envisioned.
2. Patients/care partners indicated that they are worried that treatments may not be developed in time to help them. The number of previously conducted but unsuccessful clinical trials is disheartening.
3. Several patients noted the financial burden of IBM, which can be daunting. Patients with advanced disease will need assistance with activities of daily living – first from family members and then from hired help on a part- or full-time basis. Over time, patients need assistive devices, power wheelchairs, van conversions, stair lifts and home renovations to allow accessibility. Others may need to move into nursing homes to get the care that they need. These expenses can easily total hundreds of thousands of dollars and are rarely covered by insurance.
4. Financial concerns and an uncertain future are a particular issue for patients who retire early as they are unable to work, who live alone, or who do not qualify for disability benefits.

**There is no FDA approved treatment for IBM. IBM patients are eager to participate in clinical trials, but very few have been able to do so.**

1. In the absence of an approved pharmaceutical or surgical treatment, exercise is generally recommended to help patients maintain and potentially strengthen what function they have retained.
  - a. Physical therapy and exercise can be helpful at all stages of disease.
  - b. Occupational Therapy, often involving use of assistive devices including orthoses, canes/walking sticks, walkers, rollators, scooters and power wheelchairs, can help maintain independence and mobility while reducing fall risk.
  - c. Speech Therapy to manage dysphagia is often helpful, and esophageal dilation or other procedures can provide temporary benefit. A feeding tube may become necessary.

2. In the absence of available treatments and given the severity of the disease, it was reported that persons with IBM have been desperate enough to try unproven and potentially unsafe therapies including stem cells and ketamine.
  3. Patients are very interested in participating in clinical trials, both for the potential personal benefit and the opportunity to help advance science and assist future patients. Many patients express frustration with enrollment criteria as their disease has progressed sufficiently that they no longer qualify.
4. The patients who have had clinical trial experience have found the experience to be valuable, and one patient reported having achieved measurable benefit from his involvement in the Follistatin clinical trial.
5. One patient described the restoration of mobility function that he received from a brief trial of a medical device described as an exoskeleton. The product is approved in Canada and was recently cleared for sale in the European Union, but is not available in the United States. (This was a topic of discussion during the Q&A session.)

**While a cure and complete reversal of disease would be ideal, IBM patients and their care partners seek and expect more modest gains from treatment.**

1. Several patients expressed their primary goal of maintaining independence and mobility.
2. In general, while regrowth of muscle would be desirable, stability at the current stage would be quite acceptable for patients at early and mid-stages of disease. A treatment that slowed disease progression would also be welcomed.
3. Given the lack of treatments, patients appealed for a generous benefit/risk assessment, stating clearly that they would be interested in assuming a relatively large risk for a chance to improve or maintain function and quality of life.

**From the clinician's perspective – IBM is a challenging disease to diagnose, treat and research.**

1. IBM is not well known outside of the specialty centers, and the symptoms may be mistaken for normal aging. This can lead to significant delays in diagnosis, with a median duration of 5 years reported from initial contact with the health care system to a definitive diagnosis. Of note, making the diagnosis can be difficult as while there are diagnostic criteria, there is not a definitive laboratory test.
2. While it can be rewarding to help make the diagnosis, clinicians find it frustrating to not be able to offer treatments.
3. Physicians who specialize in IBM are convinced that the disease does shorten life, particularly in those who experience dysphagia. The connection to aspiration pneumonia is seen as the key link. Several publications based on available data support this concept. Additional long term data is required to better understand and quantify the affect of the disease on lifespan.
4. There is no shortage of available qualified patients to enroll in clinical trials. There is a significant limitation in the number of trials and therefore the patients who can be enrolled.

5. IBM trials to date have been unsuccessful. There are many potential contributors:
  - a. Incomplete understanding of cause and natural history of IBM
  - b. Duration of trials may not be adequate given slow progression
  - c. Insufficient power due to relatively small study size
  - d. Currently used endpoints may not be sufficiently sensitive to measure disease progression.
6. Historically, IBM has received relatively low levels of basic research funding, and this has contributed to the lack of progress towards treatments. More specifically, IBM related projects received a small fraction (i.e. less than 1%) of the NIH funding provided to diseases such Amyotrophic Lateral Sclerosis (ALS) or Duchenne Muscular Dystrophy (DMD) despite a similarly sized patient population (estimated at ~20,000 patients in the US).

### **FDA shared their interest in advancing clinical science towards developing treatments.**

1. Participating FDA staff thanked the participants in the session for sharing their experiences and noted the following as it relates to FDA actions in Medical Product Development:
  - a. IBM is taken seriously at FDA, similarly to other, more common neurological diseases
  - b. FDA is committed to approving products that provide meaningful benefit to patients. The discussions in this session have provided important context for that evaluation. While the Agency understands that a cure would be ideal, it is open to considering products that provide benefits such as stabilizing the disease or slowing its progression.
  - c. FDA is well acquainted with the importance of flexibility when evaluating the benefit/risk balance for serious, rare diseases that have no approved treatments such as IBM.
2. FDA noted that IBM is not well understood and that this hampers the development of therapies. The comments made by FDA echoed the issues noted by Dr. Lloyd in clinical development, including incomplete understanding of the cause and pathology of IBM, lack of alignment on targets for treatment, lack of biomarkers, and potential insensitivity of endpoints given a slowly progressing disease.
3. FDA suggested that a well designed and executed natural history study could contribute greatly to developing a better understanding of IBM and support further advances in clinical design and development. An ideal study might include the following attributes:
  - a. Enroll patients from several specialty clinics to help ensure consistency and standardization of data collection procedures and a sufficiently large patient population
  - b. Create a thorough and well thought out trial questionnaire that collects data that accurately tracks disease progression and could contribute to potential outcome measures
  - c. Gather at least two years data for initial analysis
  - d. Enroll a sufficiently large population to enable analysis.
  - e. Share the database broadly to allow for multiple analyses from varied outside perspectives.

### **Questions**

Dr. Lloyd was asked about the number of multicenter trials underway at Johns Hopkins and also about whether clinical sites were aligned to form an IBM clinical trial network. He responded that there was currently one multicenter trial underway at JHU.

He noted that a group of potential investigators have collaborated on a grant application to the NIH and

the Muscular Dystrophy Association to conduct a natural history study with many of the attributes outlined by FDA. These applications have been favorably reviewed but have not received funding. The NIH proposal is being revised to address the reviewer comments and will be resubmitted this year.

Dr. Lloyd and Ms. McGowan asked whether it would be possible for FDA to assist in providing input on choosing outcome measures for the study.

Mary McGowan made mention of TMA's interest in collaboration with NORD on a patient registry.

### **FDA divisions represented**

#### *Office of the Commissioner*

- Patient Affairs Staff (organizer)
- Office of Clinical Policy and Programs
- Office of Orphan Products Development

#### *Center for Drug Evaluation and Research (CDER)*

- Division of Neurology Products I
- Division of Neurology Products II
- Office of Neuroscience
- Office of New Drugs
- Division of Biometrics

#### *Center for Biologics Evaluation and Research (CBER)*

- Office of the Director

#### *Center for Devices and Radiologic Health (CDRH)*

- Office of Strategic Partnerships & Technology

### **Persons with IBM and Care partners represented**

TMA is grateful to the individuals living with IBM and their care partners who participated in this session as representatives of the larger IBM community:

- Bitsy and Terry Anderson, Person with IBM and Care partner
- Martha Arnold, Person with IBM
- Augie and Leslie DeAugustinis, Person with IBM and Care partner
- Ed Horack, Person with IBM
- Camille Lesoine, Care partner to Ray Lesoine, Person with IBM
- Jim Mathews, Person with IBM
- Carl and Sharon Minkovitz, Person with IBM and Care partner
- Dave and Peg Mochel, Person with IBM and Care partner
- Alexis Redmond, Person with IBM

### **Health Care Professionals represented**

- Thomas E. Lloyd, MD PHD; Associate Professor of Neurology and Neuroscience at Johns Hopkins University; Co-Director of the Johns Hopkins Myositis Center; Currently Chair of the Research Committee of TMA's Medical Advisory Board

- Lisa G. Rider, MD; Deputy Chief, Environmental Autoimmunity Group, National Institutes of Health; Former Chair of TMA's Medical Advisory Board.

### **Disclosure**

The Myositis Association disclosed that a grant had been received from EveryLife Foundation and was used to partially defray travel expenses for those participating in the session.

*Discussions in FDA Rare Disease Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report summarizes the input provided by patients and patient representatives at the meeting. To the extent possible, the terms used in this summary to describe specific manifestations of Inclusion Body Myositis, health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire Inclusion Body Myositis patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.*