FDA Patient-Led Listening Session Summary - VCP disease / IBMPFD

Tuesday, May 5, 2020 2:30 PM ET – 4:00 PM ET
Conducted online through WebEx call

I. Objective of Session

- Introduce VCP (Valosin Containing Protein) disease, originally known as IBMPFD (Inclusion body myopathy, associated with early onset Paget's disease of bone and frontotemporal dementia).
- Introduce Cure VCP Disease, Inc. (https://www.curevcp.org) the only patient advocacy organization, strictly focused on VCP disease. Review the efforts that Cure VCP Disease is driving for VCP disease.
- Share families' stories to familiarize the FDA with the phenotypes and burden of the disease

II. Summary of Topics Discussed

Speaker 1, CEO of Cure VCP Disease:

- **Family History**
  - Shared family history and seeing his mother develop the disease. See *Section V. – Patients Represented* for more information.
  - Fully disabled at age of 44
- **Cure VCP Disease**
  - Started in February 2018 in response to a potential clinical trial that never materialized
  - The core mission of the organization is to identify patients, educate the scientific and medical community of the disease and help drive therapeutic development efforts
  - A strong medical advisory board
    - Dr. Ming Guo – UCLA
    - Dr. Virginia Kimonis – UC-Irvine
    - Dr. Chris Weihl – Washington University, St. Louis
  - Strong affiliations and relationships with other rare disease and neuromuscular advocacy organizations
- **Basic science of VCP disease**
  - Originally called IBMPFD and also referred to as multisystem proteinopathy as it can have disparate phenotypes that affect multiple body systems, even in family members with the same VCP gene variant
  - The name VCP disease is inclusive of affected systems and disparate phenotypes
  - Currently, 50+ known VCP gene variants
  - Adult onset and autosomal dominant
  - Prevalence is unknown as many patients are misdiagnosed or family members refuse to get genetically tested due a lack of therapies
  - Estimate around 2,000
  - Patients can get one, two, three or even four of the following disparate phenotypes:
    - Inclusion Body Myopathy – 90%
    - Early onset Paget's disease of bone – 50%
    - Frontotemporal dementia – 30%
    - ALS – 10%
    - Parkinsonism – 4%
    - CMT - Unknown
  - Shared therapeutic development companies where repurposing opportunities might exist in the future

- **Cure VCP Disease Patient Registry**
    - Shared basic information about the Cure VCP Disease Patient Registry hosted by CoRDS at Sanford Research and created in June 2018.
    - Global, IRB approved, HIPAA and GDPR compliant
    - Patient reported annually with 69 questions
    - Currently, 59 registrants and working hard to drive more registrants
        - Uses HealthMeasures PROMIS bank questions in five sections: Global Health, Cognition, Regular functions, Lower extremity functions, Upper extremity functions
    - Shared results from eight of the demographic and ability questions
    - Patients start lowering their rating of quality of life starting in mid-40's
    - IBM patients start having difficulties in their mid-40's
    - FTD patients show cognition difficulties in 50's
- **Goals for this session**
    1. Grow education and awareness of VCP disease with FDA and scientific community
    2. Ensure that the FDA knows that the VCP disease patient population is ready and willing to participate in any clinical trials that might become available

Speaker 2

- **Family History**
    - 11 members of her family affected by VCP disease
    - Described father's diagnosis journey from ALS, Muscular Dystrophy, SMA until told there wasn't a name for his disease
    - Milestones of Speaker 2's father:
        - When Speaker 2 was in grade school, her father had issues with walking up stairs and getting out of a chair
        - When Speaker 2 was in middle school & high school, her father used a lift chair, bed was on cement blocks, walk-in shower, toilet seat had lift extension
        - When Speaker 2 was a junior in high school, her father moved into Iowa Veteran's Home
        - Shortly thereafter, he began using electric wheelchair
        - Kept getting weaker and had to use puff straw to control wheelchair
        - Couldn't use hands, bathe himself, go to bathroom by himself, comb hair, feed himself or brush teeth
        - Passed away at age 67
    - Aunt with disease
        - Showed symptoms in early 50's when began falling, muscle weakness and incontinence.
        - Her doctor genetically tested and found the VCP gene mutation that explained all of the family issues
        - Aunt's daughter is caregiver who checks on her 1-2 times per day. Aunt's daughter has tested positive for VCP disease though no symptoms yet
        - Suffers from depression due to loss of independence from disease and attempted suicide in fall of 2019.
- **Personal Challenges**
    - Speaker 2 tested positive once family discovered VCP gene mutation was the cause
        - Currently has weakness in shoulders and high levels of anxiety
        - Has four children and has not yet told them. Some of the children have special needs
        - Doesn't want her children to be afraid and worry about their mother, especially as there are no current treatments
        - Tries hard to not show muscle weakness, but getting harder

        - Goal for participating in this teleconference is to share her family's journey and the struggle
        - Is willing to do whatever is necessary to help find a treatment

Speaker 3

- **Family History**
    - Extensive family history with VCP disease
        - Comes from large family. 14th of 15 children. 8 siblings have VCP disease.
        - 3 year diagnosis journey started with high levels of CPK
        - After additional testing with no conclusions, at age 52, a muscle biopsy was performed with a diagnosis of LGMD
        - After a genetic test, discovered it was VCP disease
        - Maternal grandmother died at 73 from VCP disease related symptoms
        - Mother died at 75 of VCP disease related symptoms
        - Some family members have been genetically tested, others have not. Most likely have aunts/uncles and cousins affected
- **Personal Challenges**
    - Personal struggles with VCP disease
        - Gone from using cane and AFO to walker and scooter
        - Climbing stairs, long walks and physical activity is extremely difficult
        - In constant pain and soreness
        - Exercise is a catch-22
            - No exercise muscles atrophy and tighten
            - Too much exercise causes soreness and higher propensity to fall
        - Challenged to dress self and wife has to help with buttoning shirt
        - Getting up from chair and going to bathroom is difficult
        - Difficulty sleeping and turning in bed
        - Get bad leg and foot cramps, discomfort, and anxiety
        - Have a lot of adrenaline and with lack of mobility, have difficulty releasing this adrenaline
    - Feel blessed
        - Thankful for job, providing for family and that it is not a physical job
        - Employer provides support and resources to work from home as needed
        - Hopeful that FDA will assist VCP disease patients in finding therapeutic advancements

Speaker 4

- **Family History**
    - Fulltime caregiver for his mother, who has had FTD for the past five years
    - Speaker 4 quit college to care for his mother so that his sister could finish high school and now college
    - Mother was a skilled oncology nurse and case manager for 33 years
    - In the beginning, symptoms were very subtle, but became more noticeable and alarming
        - Speech changes; incorrect use of words
        - Emotional changes; intensive highs and lows
    - Seizures became more common and she was forced to go on disability leave
        - Admitted to hospital 16 times for seizures
    - After 3.5 years, UCSF successfully identified VCP gene mutation through whole exome gene test
    - Speaker 4 became solely responsible for paying bills, planning meals and grocery shopping as mother was unable to do so. Also is responsible managing all aspects of her care.
        - Mother is unable to communicate

        - Must take her to bathroom every 1.5-2 hours to avoid accidents
        - Must be prompted to drink fluids
    - "All of these things especially toileting and bathing are things I never thought I would need to do for my mom"
- **Personal Challenges**
    - Speaker 4 has put life on hold to care for his mother. Because he has not finished his advanced education, his time is worth less than what it would cost someone else to care for his mother
    - Does not have much of a social life as he must remain available for his mother
    - Family history
        - 10 family members, including mother and deceased family members have/had FTD phenotype of VCP disease
        - None, other than mother, have been officially genetically tested as the VCP discovery has been recent
        - Grandmother, over six years, gradually deteriorated from FTD symptoms having increased seizures. Her last 29 days of life were spent without hydration or nutrition.
        - This will be a similar conclusion to their mother's life
    - The Future
        - Both Speaker 4 and his sister could inherit the VCP gene mutation. This weighs on them
        - How do they proceed on marriage, children, etc.?
        - Sister will graduate in early May from college
        - There is anxiety about the future
        - There is sadness in not being able to know mother while becoming young adults

Speaker 5

- **Family History**
    - Seven members of family with symptoms related to VCP disease
    - Aunt was first family member to show symptoms
        - Death certificate listed Paget's disease and Alzheimer's
        - Alzheimer's was most certainly misdiagnosed as her behavior was very erratic towards end of life
    - Mother was second family member to show symptoms
        - Mom initially had falls and used cane/rollator
        - Then displayed erratic behavior and ended up exhibiting all phenotypes of VCP disease
        - After one particular episode, she was moved into an assistive living facility where she lived for two-and-a-half years before passing
        - Mom though still ambulatory, lost language and was no longer the "life of the party"
    - Cousin was third family member
        - Quick witted and intelligent, but suddenly started having bizarre behavior
        - Diagnosed with Parkinson's at age 35
        - Fired from job and couldn't complete most basic of tasks
    - Oldest brother
        - Muscle weakness and personality changes
        - Originally diagnosed at Inclusion Body Myositis
        - Before his death was non-ambulatory, had severe case of FTD and a 24 hour caregiver

- **Personal Challenges**
    - Speaker 5 started experiencing symptoms about 11 years ago
        - Tripping and falling, losing balance and having urinary incontinence
        - Original diagnosis was PPMS as she has the Babinsky reflex, but brain MRI and lumbar puncture were normal
        - Misdiagnosis journey lasted 8 years until going to Mayo and getting genetic test that confirmed VCP disease
    - Speakers 5's sister has VCP disease, but only exhibits the Paget's disease of bone phenotype
    - Speaker 5 and her sister recognized early on that there was something going on in family and that they would likely inherit this mystery disease
    - She and her sister purchased long term care policies
    - Today
        - Biggest challenges are walking and not falling. Horrible balance.
        - Use scooter if needing to walk long distances
        - Getting dressed in the morning is challenge
        - Left hip flexor is so tight, that can't lift left ankle to put right knee to get a shoe or sock on
        - Need walk in showers as can't lift legs to get into a tub
        - Recently went on a cruise and friend had to help Speaker 5 get in/out of the tub
        - Getting feet under the covers in bed is a struggle, let alone trying to turn over.
        - Have a neurogenic bladder and issues with bowels. Accidents are very stressful
    - Unable to go to PT and stretch zone due to pandemic. This is important to staying ambulatory
    - Fear of losing independence, especially driving
    - Speaker 5 and sister never got married, nor had children and are thankful that they will not pass on VCP disease
    - Concerned about extended family members that have not been tested and have a chance of getting VCP disease
    - More neurologists, rheumatologists and endocrinologists need to know about this disease. Many patients are being misdiagnosed
    - Asking the FDA to assist in efforts for a therapeutic treatment

III. Partner Organization

- Cure VCP Disease, Inc. helped identify and prepare all speakers
- Cure VCP Disease, Inc. also invited members of the rare disease, neuromuscular disease and frontotemporal dementia communities to participate in the listening session. The following organizations were listeners of the meeting:
    - Jain Foundation (https://www.jain-foundation.org)
    - Muscular Dystrophy Association (https://www.mda.org)
    - National Organization for Rare Disorders (NORD) (https://www.rarediseases.org)
    - The Association for Frontotemporal Degeneration (https://www.theaftd.org)
    - The Speak Foundation (https://www.thespeakfoundation.com)

IV. 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
- Office of Translational Sciences, Division of Biometrics
- Rare Disease Program
- Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (ORPURM), Division of Rare Diseases and Medical Genetics (DRDMG)
- Clinical Outcome Assessment Staff

Center for Biologics Evaluation and Research (CBER)
- Office of the Director

Center for Devices and Radiologic Health (CDRH)
- Office of Strategic Partnerships & Technology
- Office of Product Evaluation and Quality (OPEQ), Office of Health Technology 2

Non-FDA Participants
- The Reagan-Udall Foundation for the FDA

V. Patients Represented

- **Speaker 1** – Male VCP disease patient with IBM phenotype
    - Age 44, diagnosed at 39
    - Grandmother, mother (diagnosed) and aunt (diagnosed) deceased from VCP disease symptoms
    - Two uncles (diagnosed) with VCP disease symptoms still living
- **Speaker 2** – Female VCP disease patient with IBM phenotype
    - Age 41, diagnosed at 39
    - Father, sister (diagnosed), uncle, grandfather, great grandmother and great, great aunt deceased from VCP disease symptoms
    - Aunt (diagnosed), two cousins (diagnosed) and one niece (diagnosed) with VCP disease symptoms still living
- **Speaker 3** – Male VCP disease patient with IBM phenotype
    - Age 58, diagnosed at 52
    - Mother, sister, brother (diagnosed), and grandmother deceased from VCP disease symptoms
    - Four sisters (two diagnosed), two brothers (one diagnosed) with VCP disease symptoms still living
- **Speaker 4** – Male VCP disease caregiver for mother with FTD phenotype
    - Age 24, caring fulltime for mother since age 19
    - Grandmother, great-grandmother, great-great grandmother and six other family members deceased from VCP disease symptoms
    - Mother (diagnosed) was first VCP disease diagnosed family member
- **Speaker 5** - Female VCP disease patient with IBM and Paget's phenotype
    - Age 61, diagnosed at 57 (eight year diagnostic journey)
    - Mother, brother (diagnosed), aunt, grandmother, and two cousins deceased from VCP disease symptoms
    - Sister (diagnosed) with VCP disease symptoms, Paget's disease, still living

VI. Financial Interest

None of the participants in the Listening Session received funding from Cure VCP Disease for travel or participation. Additionally, Cure VCP Disease, nor the speakers, received any funding from any sponsor for participation in this Listening Session.

VII. Disclaimer

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 reflects Cure VCP Disease's account of the perspectives of patients and caregivers who participated in the Rare Disease Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of VCP disease, 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 VCP disease patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.