

## **Public Comment**

### **Lily Chu, MD, MSHS**

Thank you for this opportunity to address CFSAC members and attendees. At the end of April, I was invited by the US Food and Drug Administration to participate in their Drug Development Workshop as a patient representative and as a board member of IACFS/ME. To answer some of the questions FDA posed, Dr. Leonard Jason and his team helped me design and analyze an online survey. This is a summary of the results we have up to mid-April from 360-470 US residents with a self-reported clinician-confirmed diagnosis of CFS or ME.

#### Demographics:

85% of our subjects were female and almost all subjects were Caucasian. The average age was 51 and the average duration of illness was 18 years.

#### Symptoms:

The 5 most significant symptoms patient reported were fatigue, post-exertional malaise, pain, sleep, and cognitive problems. Symptoms that haven't been studied as much such as multiple chemical sensitivities, gastrointestinal symptoms, and orthostatic intolerance were also deemed to be significant by over 50% of our subjects..

99% felt that their illness was not improving over time, citing worsening of existing symptoms and appearance of new symptoms.

We asked about five tests that ME/CFS specialists commonly order to assess their patients – natural killer cell activity, repeated cardiopulmonary exercise test, brain imaging, neuropsychological testing, and tilt table. For each test, between 40%-60% of respondents had never had the test before due to cost, insurance coverage, and/or physician ignorance/ resistance to ordering a test.

Of those who had any of the five tests, 66% had at least one abnormal result. For natural killer cell activity, for example, 70% noted an abnormal result. For tilt table testing, 80%. The high percentages of patients with abnormal tests suggest that these tests should be considered for coverage by health insurance to help clinicians better assess and treat their patients. In fact, in the section on diagnostic workup in the current CDC CFS education module, brain MRI and tilt table testing are mentioned as tests to consider if symptoms are present.

#### Impact on Daily Life:

Using a standardized measure of physical functioning, we found our respondents to be more disabled, on average, than the average patient with chronic lung disease or congestive heart failure. Only 13% were employed, with almost all citing ME and or CFS as the reason for why they could not work. For even basic personal care, 89% needed assistance or had to change their pre-illness routine. On their worse days, 60% were bedridden. On their best days, 75% were primarily homebound and could only do some light housework or less.

#### Perspectives on Current Treatment:

75% of people felt current treatments were not helpful or only slightly helpful but not enough to improve their day-to-day function. Patients repeatedly wrote about the need for disease-modifying treatments and not only for treatments that helped control symptoms.

We asked about how well currently recommended treatments worked the illness overall and for three common symptoms: sleep, pain, and cognitive problems.

These treatments were cited as helpful by more than 50% of subjects:

- for the overall illness - balancing rest with activity, restricting or modifying physical/ mental activities
- for sleep – CPAP, over-the-counter medicines, zolpidem, eszopiclone, TCAs, trazodone, benzodiazepines
- for pain – short/ long-acting opioids, flexeril, ibuprofen

Some alternative/ complementary/ non-drug treatments such as massage and meditation/ relaxation for pain also made the cut. Helpful prescription drugs cited in patient comments included gamma-hydroxybutyric acid for sleep, lisdexamfetamine for thinking, tizanidine/ baclofen for pain, and midodrine/ flunarizine/ beta-blockers for orthostatic intolerance. In contrast, exercise programs, administered by a professional and part of the current standard of care, were noted by 62% as worsening their health.

In our short survey, we were unable to explore details and co-morbidities but the finding that over 50% of subjects found opioids to be effective for pain and benzodiazepines to be effective for sleep suggests that health insurance coverage for these medications for some CFS patients should be considered especially if other treatments fail.

The main reasons cited for stopping a medicine were side effects followed by decrease in effectiveness over time, especially with sleep medications. For effective non-drug treatments, cost and insurance coverage were major reasons for discontinuation. Respondents were also concerned being more sensitive to drugs and the dependency potential of some medications.

I am out of time so please refer to the written testimony and table I have submitted to CFSAC for further details. My contact information is on the table. We are continuing to examine the data and will submit a report to the FDA docket related to the Drug Development Workshop in August. Thank you for your attention.

#### Limitations:

Since this is an online survey using self-reported clinician-confirmed diagnosis of CFS or ME, we were unable to personally confirm exactly who had CFS or ME. About 6% of respondents stated they were self-diagnosed or did not have CFS or ME and were not counted in the results.

The overwhelming majority of respondents to our survey self-identified as Caucasian and over 50% possessed at least an undergraduate college degree. This is likely a result of adequate access to care to obtain an accurate diagnosis, Internet access, and membership in support groups rather than an accurate reflection of the epidemiology of ME or CFS. In fact, multiple community-based studies suggest a higher prevalence and more severe morbidity in minority populations. Thus, our survey results may not be generalizable to non-Caucasian or lower socio-economic groups.

We did ask about antibiotics, antivirals, and immunomodulators but 1) answers were rather mixed (side effects, not enough time on medicine due to physician/ cost, etc.) 2) sample sizes were too small to come to concrete conclusions. Also, to date, no drug was noted in open patient comments to be very successful by more than a handful of respondents. In addition given the relatively short length/ nature of the survey, we weren't able to subgroup respondents and ask how they did on various treatments, which we think is key to finding effective treatments.