MTV: The Real World

As you may be aware, this season's cast of the MTV reality show, The Real World, includes a young woman with cystic fibrosis (CF) who smokes. The Real World is a long-running series that is very popular among teenagers and young adults. It chronicles the day-to-day lives of 7 young men and women who live together in a house over the course of several months.

Some of you have reported that your patients and their families feel compelled to educate the MTV audience about CF and the extreme dangers smoking presents for someone with the disease. Although the CF Foundation has made several attempts to contact MTV to request that they include an educational statement at the start or the end of each episode, MTV has not responded.

If your patients or families wish to contact MTV directly, here are both the mailing address and the phone number for MTV's headquarters:

MTV Viewer Relations
1515 Broadway, 23rd Floor
New York, NY 10036-5702
(212) 258-8000

The CF Foundation recommends that MTV make more information available to its viewers about CF and the dangers of smoking for people with the disease. This could be done in any of the following ways:

- A follow-up special about CF and the dangers of smoking for people with chronic lung diseases;
- A disclaimer at the beginning or the end of each episode about the dangers of smoking for people with lung diseases;
- A banner at the beginning or the end of each episode that directs people to the CF Foundation's Web site for more information on CF and how they can help; and/or
- Similar content on the MTV Web site.

We hope the above information is helpful; feel free to pass this on to your patients and families. If you have any questions, please contact Leslie Hazle (lhazle@cff.org <mailto:lhazle@cff.org>).

Center Focus

Summer, 2004

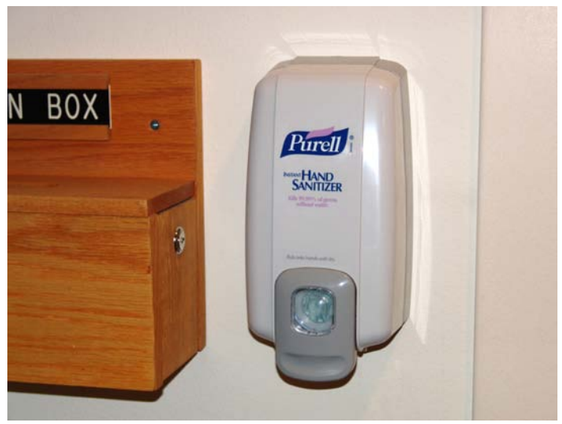
Newsletter of the Cystic Fibrosis Center
University of Wisconsin Clinical Sciences Center

Welcome to another edition of the University of Wisconsin Cystic Fibrosis Center newsletter. There has recently been a flurry of wide-reaching announcements from the Cystic Fibrosis Foundation. Some of you may already be aware of these by monitoring the Cystic Fibrosis Foundation's website at *http://www.cff.org*. For those of you who do not have internet access, we are reproducing information on three topics from the Cystic Fibrosis Foundation: pancreatic enzymes, the press release of encouraging information of the Inspire Pharmaceuticals drug INS37217, and information about curcumin.

Infection Control

In the last issue of the CF Center newsletter, we highlighted some infection control guidelines. Here are more specific guidelines for infection control in the waiting room:

1. A dispenser for the Purell waterless antiseptic gel has now been installed on the wall of the pediatric waiting room next to the Suggestion Box. A dispenser will also be installed in the waiting room of the adult pulmonary clinic. Patients and family members should use the alcohol-based hand rub upon arrival to the waiting room.



2. Patients should attempt to remain a minimal distance of three feet from other patients in the waiting area.
3. If patients need to cough, they should cough into a tissue and immediately discard this into the garbage can and then repeat hand hygiene using the alcohol-based hand rub.
4. Antibacterial wipes will be available adjacent to the touch-screen computer game and desktop computer in the pediatric waiting room. Please use an antibacterial wipe to clean the touch-screen computer game and keyboard and mouse prior to using these devices.
5. The Purell alcohol-based hand rub has been installed in all clinic examining rooms. Patients and families should use this again on their hands when they depart the clinic.

The Cystic Fibrosis Foundation sponsored a webcast "How To Avoid Germs In CF" on January 12, 2004. This webcast and the previous webcast ("The Patient As A Partner In Research") are archived on the Cystic Fibrosis Foundation website. You may access these webcasts by going to *http://www.cff.org* and click on the link on the left hand side of the page "Living with CF."

Screening for Diabetes

Diabetes can occur in cystic fibrosis patients who have pancreatic insufficiency. The pancreas makes enzymes to allow us to absorb protein and fat and also has cells that produce insulin. Over time, the insulin-producing cells can be replaced by scar tissue and this can result in diabetes. Although we have checked random blood sugars as part of our routine labs for many years, a more sensitive method to screen for diabetes is the oral glucose tolerance test. This involves obtaining a fasting blood sugar in the morning (in other words, a blood sugar in the morning with no prior breakfast) followed by drinking a sugar solution called Glucola, followed by a second blood sugar two hours later. It is suggested that this be considered as a screening test every two years on patients ages ten to sixteen years and annually over age sixteen years. Because many of our clinics are in the afternoon, it is not feasible to perform this at University of Wisconsin Hospital. We will be discussing this with you in future clinic visits and this test can be done through your local physician's office or hospital. There is impressive data that if diabetes is diagnosed and treated, then there is improved weight gain and improved pulmonary functions.

Room Service for Inpatients

For those patients who require admission to University of Wisconsin Hospital, there is a new concept in delivery of the meals. The hospital has switched to a room service concept in which one orders a meal and it arrives in approximately 45 minutes. Please keep in mind that airway clearance is performed prior to eating rather than after eating a meal. Therefore, airway clearance will occur when a patient calls for their meal. The airway clearance should be able to be completed prior to the meal arriving in 45 minutes.

FDA Requires Review and Approval of Pancreatic Enzyme Supplements: Information for People With CF

In April 2004, a new rule was issued requiring makers of pancreatic enzyme supplements to get their drugs approved by the Food and Drug Administration (FDA) within the next four years.

For enzymes to receive FDA approval, companies must test them in clinical trials in people with pancreatic diseases, which includes cystic fibrosis (CF). These clinical trials would confirm the safety and effectiveness of the enzymes. People with CF who take enzymes to digest their food still will be able to get their prescribed enzymes during the next four years. This document will help answer questions you may have about the FDA's rule and its possible effects on the enzymes you take.

Why did the FDA make this rule?

The goal of this new rule is to make sure that pancreatic enzymes have the right amount of active ingredients to digest food; inconsistencies in enzyme formulation can cause problems with digestion. There are several types of enzymes on the market now, which vary in what they contain, how they are made and how many pills must be taken. It is difficult to know the exact amount of active ingredients in the different enzymes. By conducting clinical trials and requiring FDA approval, the manufacturing process of pancreatic enzymes will be standardized, which ensures the consistency of the capsules from batch to batch. In addition, by having more precise information on these enzymes and how effective they are, doctors will be better able to prescribe the right amount of enzymes.

When will the rule take effect?

The FDA's rule will take effect immediately. Enzymes that are available now will likely remain so over the next four years. During this time, makers that choose to do so will conduct clinical trials to make sure their enzyme products are safe and effective. Once the clinical trials are complete, the FDA will look at the information and decide if that company's enzyme or enzymes should be approved. At the end of four years, if a maker has not received FDA approval, its enzyme product will no longer be available and your doctor will prescribe an appropriate enzyme product for you.

Why haven't enzymes been approved by the FDA before?

Pancreatic enzymes, like a number of older medications, were first made before the FDA required them to be tested in clinical trials to see how well they work. The FDA allowed these medications to be "grandfathered" products, so they could be put on the market without its review and approval. This new rule means that the FDA requires enzymes to meet the same standards of testing as any other new drug. Because of the importance of pancreatic enzymes for people with CF, the FDA will let these enzymes remain available in the meantime.

Questions & Answers

Are clinical trials of pancreatic enzymes really necessary? Isn't this a step backward?

This is a step forward in improving the quality of care for people with CF. The CF Foundation has received reports of health problems in people with CF when an enzyme product

Patient Compliance Webcast Teleconference

Join Boomer Esiason and Dr.Lynne Quittell, CF Director of Columbia University for an inspirational discussion on the importance of improving the quality of life for people with cystic fibrosis.

About the speaker

Boomer Esiason, a four time-Pro Bowl selection and the 1998 NFL Most Valuable Player who learned in 1993 that his son, Gunnar, just then two years old, had been diagnosed with CF. That same year he founded the Boomer Esiason Foundation, a partnership of leaders in the medical and business communities joining with acommitted core of volunteers to provide financial support for research aimed at finding a cure for CF. The BEF works to heighten education and awareness of CF and to provide a better quality of life for those affected by CF.

June 22, 2004 — 6 p.m. EST / 5 p.m. CST / 3 p.m. PST

June 23, 2004 — 9 p.m. EST / 8 p.m. CST / 6 p.m. PST

Topics

- My first introduction to CF
- A parent 's involvement
- Importance of therapies
- Looking and moving forward
- BEF 's commitment to CF Awareness
- Programs available for people with CF

Instructions

Go to the Link below to pre-register and to join the event at the designated event time.

www.cfcompliance.com

You will have two connection options on the day of the event.

1. You can listen via the internet by selecting the appropriate media player when you enter the lobby. Please note the your computer should be equipped with speakers or headphones as well as a standard media player such as RealPlayer or Windows Media Player in order to use this option.

2. To listen via the phone, call the audio conference dial-in number listed below.

Conference Call Dial-in number: (888)806-9460 (ask for the Cystic Fibrosis conference call)

If you have any technical problems on the day of the event, please call ON24 Customer support at (877) 934-2524

Chiron: This educational program is made possible by an unrestricted educational grant from Chiron Corporation.

Can curcumin benefit me or my child?

It is not yet known whether curcumin will benefit people with CF. Benefits seen in mice often do not occur in humans. It is important to point out that the study was conducted in mice only and that CF mice only have the digestive complications of CF, not the lung problems. Until the dosage, safety, and possible benefits for people with CF have been studied in clinical trials, the CF Foundation does not recommend curcumin as a therapy.

For now, people with CF should continue with their existing therapies as prescribed by their CF physician. Introducing any experimental therapy — including curcumin — that has not been appropriately studied could have unknown and potentially dangerous side effects. Talk with your CF physician before making any changes in your or your child's therapies.

What is the CF Foundation doing to bring curcumin to patients?

The CF Foundation funded the study on the effects of curcumin in CF mice. The results of this research were very encouraging. The mice showed signs of CFTR correction and improved survival rates. It is too soon to say if curcumin would do the same in people and if it would alter the course of disease in CF patients.

The CF Foundation is moving forward with preclinical studies in animals and also will begin a Phase I safety and dosage trial in CF patients as quickly as possible. Working with SEER Pharmaceuticals, the trial is expected to begin in the late summer/early fall of 2004.

What are the side effects of taking curcumin?

The side effects of curcumin are not yet known and is part of what will be established through clinical trials. In previous research, curcumin has been safe but these have been in patients with other diseases. Interactions between curcumin and standard CF therapies could occur and have harmful effects.

Who manufactures curcumin?

Curcumin is available from a variety of nutritional supplement manufacturers. It comes in varying concentrations, strengths and formulations and is not regulated by the FDA. Therefore, the amount of curcumin contained in these supplements is not standardized.

If curcumin is effective in CF mice, then shouldn't it also benefit people with CF?

Not necessarily. CF mice often have different reactions to therapies than people do. Because mice with CF only have the digestive complications and not the lung problems, it is hard to say if the lungs of people with CF would benefit from something that benefits the digestive systems of mice.

How can I or my child participate in the curcumin clinical trial?

The clinical trial for curcumin is being designed now. Information about CF clinical trials is regularly updated on the CF Foundation's Web site at *www.cff.org*. You also can ask your CF care team about any clinical trials that may be taking place in your area.

What other potential therapies does the CF Foundation have in the pipeline to treat or cure CF?

The CF Foundation has nearly two dozen potential therapies in various stages of preclinical development and clinical trials in its therapeutics development pipeline. Any one of these, if successful, could make a dramatic difference in the lives of those with CF. Some therapies treat the symptoms of CF, while others address the basic defect in CF cells. A list of CF Foundation-supported clinical trials and their descriptions is available on the CF Foundation's Web site at *www.cff.org*. The CF Foundation will continue to move these potential treatments forward while also adding new therapies to the development pipeline.

was used that did not work as it should. By requiring enzymes to be consistent in their formulation and to work properly, people with CF can be assured that they are getting the right amount of enzymes for their digestive and nutritional needs.

How can my child or I participate in the clinical trial of a particular enzyme product?

The clinical trials for enzymes will be designed soon. You can ask your CF care team about participation in clinical trials of enzymes or other drugs. It is critical for people with CF to participate in clinical research to help with the discovery of a drug or drugs that will improve the quality of life for people with CF. Information about CF clinical trials is regularly updated on the CF Foundation Web site at *www.cff.org*.

Will I still be able to buy the enzymes that my child or I take now?

The enzymes you or your child currently are taking still should be available for the next four years. However, the maker voluntarily can remove its enzyme products from the market before that time if they so choose. After four years, if the FDA approves your enzyme, it will remain available. However, if the maker decides not to apply for FDA approval or if the enzyme does not receive approval, your doctor will not be able to prescribe it and will work with you to prescribe a different enzyme.

How do I know which enzyme is best for my child or me?

The amount of enzymes needed for good nutrition varies from person to person. Your CF doctor will work with you to decide which enzyme is best for you or your child. The enzyme product given to you from your pharmacist may be different than that prescribed by your doctor. To minimize the possibility that you are getting a different enzyme than your doctor prescribed, ask your doctor to write "Do Not Substitute" on the prescription. Ask your doctor if you have questions about what was given to you by a pharmacist.

What happens if my insurance will not cover a different enzyme?

Once the FDA approves specific enzymes, we expect insurance will cover them according to your insurance policy. CF Services Pharmacy can help people with CF work with their insurance companies to get enzymes covered; for more information visit www.cfservicespharmacy.com or call 1-800-541-4959.

Was the CF Foundation involved in the FDA's decision?

The CF Foundation offered its expertise about CF and pancreatic enzyme supplements to the FDA. We shared our concerns about the variations and inconsistencies in the available pancreatic enzymes. We identified experts who could provide the FDA with more information about the importance of reliable and effective pancreatic enzymes for people with CF. The CF Foundation supports the FDA's decision because it will make enzymes better and help improve nutrition and digestion for people with CF. We will continue to offer our expertise to the FDA to ensure the best health for everyone with CF.

Why is good nutrition important for people with CF?

Although enzymes help people with CF digest their food, there are still many people with CF who need more help with digestion. It is important that people with CF have the energy and fat stores to help fight infection and regain strength. Several studies have shown that good nutrition can have a positive impact on the health of the lungs and the body overall. Without good nutrition, people with CF may not be able to stay as healthy as possible. The CF Foundation has a paper called "Nutrition: Pancreatic Enzyme Replacement in People With Cystic Fibrosis" available on its Web site at *http://www.cff.org/living_with_cf/child_focus.cfm* or call (800) FIGHT CF.

If the CF Foundation is focusing on enzymes, will this take away from efforts toward a cure?

No, the CF Foundation is looking at all aspects of CF research and care to ensure a better quality of life for people with CF and to find a cure. We take a broad and varied approach in the fight against CF to help ensure the success of our mission. Currently, there are nearly two dozen potential therapies being tested in the lab or in clinical trials. Many of these address the basic defect in the CF cells and could, one day, have a dramatic impact on the lives of people with CF. In the meantime, we continue to look for ways to improve the quality of life for people with CF by testing products to control and lessen the symptoms and complications associated with CF. For more information, you may visit the FDA's Web site at http://www.fda.gov/bbs/topics/news/2004/NEW01058.html

Inspire Pharmaceuticals Announces Positive Results In Cystic Fibrosis Study

Study drug was well-tolerated and demonstrated statistically significant benefit in lung function compared to placebo

DURHAM, NORTH CAROLINA – April 27, 2004 – Inspire Pharmaceuticals, Inc. (Nasdaq: ISPH) today announced top-line results in a Phase II study of INS37217 Respiratory in patients with mild cystic fibrosis (CF) lung disease. Inspire plans to present additional data from the study at the 18th Annual North American Cystic Fibrosis Conference, which will be held in St. Louis in October.

The study was a double-blind, randomized comparison of three doses of INS37217 Respiratory to placebo in 90 patients with CF at 14 clinical centers in the United States. INS37217 Respiratory or placebo was administered three times daily for 28 days by standard jet nebulizer.

The trial was designed to determine the tolerability of three times daily administration of INS37217 Respiratory in doses up to 60 mg. All three doses of INS37217 Respiratory were well-tolerated and 93% of enrolled patients completed the study. The most common adverse event was cough, which occurred in 46% of subjects overall and was comparable across all groups, including placebo.

The study was not powered to demonstrate statistically significant differences between INS37217 Respiratory and placebo with respect to efficacy. However, at the end of four weeks of treatment, subjects receiving INS37217 Respiratory had significantly better lung function compared to patients receiving placebo for FEV1 ($p = 0.006$), FEF25-75% ($p = 0.007$) and FVC ($p = 0.022$). The demonstrated benefit in FEF25-75% is particularly notable given that decline in small airway function, as assessed by FEF25-75%, is the earliest manifestation of CF lung disease. Importantly, Inspire plans to develop INS37217 Respiratory as an early intervention therapy. Inspire has received Orphan Drug Status and Fast Track designations from the Food and Drug Administration (FDA) for INS37217 Respiratory for the CF indication.

Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT), the non-profit drug discovery and development affiliate of the Cystic Fibrosis Foundation, funded the majority of the external costs for the Phase II study. Robert J. Beall, Ph.D., President and CEO of the Cystic Fibrosis Foundation and CFFT, commented, "We are delighted with these results, which far surpassed the success criteria that were set forth as part of the agreement between Inspire and CFFT. We are very pleased that Inspire will be moving forward with this exciting potential product, which addresses the basic CF defect."

The study was conducted in collaboration with the CF Therapeutics Development Network (TDN). Bonnie Ramsey, M.D., Director, TDN Coordinating Center, stated, "This is a big win for the CF community and we look forward to working with Inspire on future trials to expedite the development of this early intervention approach for CF patients."

Christy L. Shaffer, Ph.D., Inspire CEO, stated, "The results of this study exceeded our expectations and have provided important scientific support for the concept of INS37217 Respiratory as early intervention therapy. We have the resources needed to advance this program in 2004 and we look forward to continuing to work with the Cystic Fibrosis Foundation and to discussing the program with the FDA in the coming months to gain input on the overall development plan and the design of the next clinical trial."

Inspire will host a conference call and live webcast to discuss these results on Tuesday, April 27th at 9:30 am EDT. Participants in the U.S. may call (877) 780-2276 to access the call. Participants outside of the U.S. may call (973) 582-2757. The conference call will be webcast live on Inspire's website at *www.inspirepharm.com*. Replays of the conference call and webcast will be available for a limited time following the call. Replay numbers are available on Inspire's website.

About Cystic Fibrosis

Cystic fibrosis is a fatal disease involving a genetic mutation that disrupts the cystic fibrosis transmembrane regulator (CFTR) protein. This protein acts as an ion-specific channel that moves salt and water to the surface of the airways. The defect in this ion channel in CF patients leads to poorly hydrated, thick, mucous secretions in the airways and severely impaired mucociliary clearance. INS37217 Respiratory is believed to enhance the lung's mucosal hydration and mucociliary clearance mechanisms by activating an alternative ion channel that acts in the same way as the defective ion channel in moving salt and water to the surface of the airways. It is well established that mucociliary clearance is impaired early in life in CF patients, and average life expectancy for these patients is early thirties. This unique, early intervention approach is different from the approach of other approved CF products and may be important in intervening in the early clinical course of CF lung disease.

About Inspire

Inspire Pharmaceuticals, Inc. is a biopharmaceutical company dedicated to discovering, developing and commercializing novel prescription products in disease areas with significant commercial markets and unmet medical needs. Inspire has significant technical and scientific expertise in the therapy areas of ophthalmology and respiratory and is a leader in the field of P2 receptor technology with a current focus on P2Y2 and P2Y12 receptors that show therapeutic promise. Inspire's specialty sales force promotes Elestat™ and Restasis®, ophthalmology products developed by Inspire's partner, Allergan, Inc. In addition to its partnership with Allergan, Inspire has development and commercialization alliances with Santen Pharmaceutical Co., Ltd. and Kirin Brewery Co., Ltd., and has a collaboration with Cystic Fibrosis Foundation Therapeutics, Inc.

Forward-Looking Statements

The forward-looking statements in this news release relating to management's expectations and beliefs are based on preliminary information and management assumptions. Such forward-looking statements are subject to a wide range of risks and uncertainties that could cause results to differ in material respects, including those relating to product development, revenue and earnings expectations, intellectual property rights and litigation, competitive products, results of clinical trials, the need for additional research and testing, delays in manufacturing, funding and the timing and content of decisions made by regulatory authorities, including the United States Food and Drug Administration. Further information regarding factors that could affect Inspire's results is included in Inspire's filings with the Securities and Exchange Commission. Inspire undertakes no obligation to publicly release the results of any revisions to these forward-looking statements that may be made to reflect events or circumstances after the date hereof.

Curcumin: Information for Patients and Families

In April 2004, researchers from Yale University and the Hospital for Sick Children in Toronto, funded by the National Institutes of Health and the Cystic Fibrosis Foundation, published the results of a study on the effects of curcumin in cystic fibrosis (CF) mice with the DeltaF508 mutation of the CF gene. The CF Foundation also announced concurrently that it is working with SEER Pharmaceuticals to begin a safety trial of curcumin in people with CF. This fact sheet answers questions about curcumin and the CF Foundation's clinical trial plans. The CF Foundation advises against taking curcumin until studies on its safety and effectiveness can be completed.

What is curcumin?

Curcumin is a component of the spice, turmeric, and is what produces its bright yellow color and strong taste. Although curcumin is available as a nutritional supplement in health food stores, these supplements are not approved by the Food and Drug Administration (FDA). Therefore, the purity and quality of such supplements is not known and they may contain other ingredients of unknown origin. The additional ingredients also may mask any potential beneficial effects of curcumin.