Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/breaking-rcdi-cycle-microbiome-strategy/35918/

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An Expert's Approach to a Difficult-to-Manage Condition: Breaking the rCDI Cycle with a Microbiome-Focused Strategy

ReachMD Announcer:
You're listening to ReachMD, and this Medical Industry Feature, titled "An Expert's Approach to a Difficult-to-Manage Condition: Breaking the rCDI Cycle with a Microbiome-Focused Strategy," is sponsored by Nestle HealthScience. And now, here's Dr. Paul Feuerstadt.

Dr. Feuerstadt:
When I'm asked by colleagues why I'm passionate about finding new ways to approach recurrent *C. difficile*, I tell them about my patients. I discuss the enormous physical and emotional burden that patients and caregivers can experience when *C. difficile* becomes a vicious cycle.

I've seen patients lose productivity and independence. I've seen them lose confidence and their desire to see their friends and family because they're afraid of being away from a bathroom or are nervous about spreading the infection to others. This is why the fight against recurrent *C. difficile* matters so much to me.

Hi, my name is Dr. Paul Feuerstadt. I am an attending Gastroenterologist at the PACT Gastroenterology Center, and an Associate Clinical Professor of Medicine at the Yale University School of Medicine. I act as a paid consultant for Nestle Health Science, and I have been compensated for my participation in this video and related promotion of VOWST.

I have been practicing medicine for more than 20 years and my research and lectures focus heavily on chronic diarrheal syndromes, with the specific focus on *clostridioides difficile* infection, or *C. diff*, and recurrent *C. difficile*, an even greater challenge than primary *C. difficile*, which is what I'd like to talk about today.

The burden of *C. difficile* is well known and has been a growing issue for years. The Centers for Disease Control and Prevention has labeled *C. difficile* an urgent public health threat, and its recurrence can lead to clinical, social and economic burden. The risk of recurrence after a primary infection is as high as 25% but what is more alarming, is that it may be as high as 65% after two episodes.

Recurrent *C. difficile* poses a clinical challenge that is distinct from primary infection. To better understand this, it's important to mention that the gastrointestinal microbiome is believed to play a pivotal role in providing colonization resistance. The leading risk factor for *C. difficile* infection is exposure to broad spectrum antibiotics, which can disrupt the diverse ecosystem of the gastrointestinal microbiome. Primary *C. difficile* infection is treated with antibiotics. Typically, vancomycin and fidaxomicin, which can cause dysbiosis or alterations in the colonic microbiota. And in many cases, following antibiotic treatment, the deficient microbiota is unable to fully replenish itself.

Dysbiosis, or alteration of the colonic microbiota, can enable an environment that favors spore germination, resulting in recurrent *C. difficile* infection. And continued disruption of the microbiota caused by repeated cycles of antibiotic therapy used to treat recurrence, leaves patients vulnerable to even more recurrences. And that's how they can find themselves in a vicious cycle of recurrence.

Now, let's review the indication and limitation of use for VOWST.

INDICATION
VOWST is indicated to prevent the recurrence of *Clostridioides difficile* infection (CDI) in individuals 18 years of age and older following antibacterial treatment for recurrent CDI (rCDI).

Limitation of Use: VOWST is not indicated for treatment of CDI.

Taking a bimodal approach to prevention of recurrent *C. difficile* can be important, because if you're only treating the infection with an

antibiotic, then you're only addressing half of the problem. Antibiotics can kill toxin-producing bacteria in the vegetative phase of *C. difficile*, but they can't kill *C. difficile* spores. And while your patients may show clinical improvement while taking the standard of care antibiotic, they can be left with a decreased level of microbiome diversity. This is where VOWST comes in. It is thought to rapidly facilitate restoration of the gut microbiome and inhibit the spore germination that can perpetuate the cycle of *C. difficile* recurrence.

The mechanism of action of VOWST has not been established. Because the antibiotic can treat the vegetative but no the spore phase of recurrent *C. difficile*, it's important to address both phases of recurrent *C. difficile* by using a dual approach of VOWST following antibiotics.

Now, let's take a moment to review some of the important safety information for VOWST.

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS
Transmissible infectious agents: Because VOWST is manufactured from human fecal matter, it may carry a risk of transmitting infectious agents. Report any infection that is suspected to have been transmitted by VOWST to Aimmune Therapeutics Incorporated at 1-833-246-2566.

Potential presence of food allergens: VOWST may contain food allergens. The potential to cause adverse reactions due to food allergens is unknown.

There are several options for the prevention of recurrent *C. difficile*, but VOWST is the first and only FDA-approved, orally administered, microbiome therapeutic used following antibiotics proven to prevent *C. difficile* recurrence. VOWST, used following antibiotics, was studied in a rigorous Phase 3 clinical development program.

ECOSPOR 3 was a multicenter, randomized, double-blind, placebo-controlled parallel group trial in adults 18 years of age or older with recurrent *C. difficile* infection. The primary endpoint was recurrence at 8 weeks, and secondary endpoints were adverse events within 24 weeks and recurrence at 4, 12, and 24 weeks, based on the intent-to-treat population. The trial included 182 adults with 2 or more *C. difficile* recurrences. Eighty-nine participants received VOWST following antibiotics and 93 participants received placebo following antibiotics.

In ECOSPOR 3, VOWST, following antibiotics, demonstrated superior and durable prevention of *C. difficile* recurrence when compared to treatment with an antibiotic alone. At 8 weeks, 88% of participants who took VOWST following an antibiotic, were recurrence-free versus 60% of participants taking an antibiotic alone. And the results were durable through 6 months, with 79% of VOWST-treated participants recurrence-free at the 6-month conclusion of the study, compared with 53% of participants on an antibiotic alone.

You can see the significant difference that VOWST made in preventing recurrence in these study participants. VOWST taken after antibiotics was generally well-tolerated. Here, you can see the safety data from the ECOSPOR 3 study.

Once again, let's review some additional important safety information for VOWST.

IMPORTANT SAFETY INFORMATION
ADVERSE REACTIONS
The most common adverse reactions (reported in ≥5% of Vowst-treated participants, and at a rate greater than placebo) were abdominal distension (31.1%), fatigue (22.2%), constipation (14.4%), chills (11.1%), and diarrhea (10.0%).

To report SUSPECTED ADVERSE REACTIONS, contact Aimmune Therapeutics at 1-833-AIM-2KNO (1-833-246-2566), or the FDA at 1-800-FDA-1088, or visit www.fda.gov/MedWatch.

DRUG INTERACTIONS
Do not administer antibacterials concurrently with VOWST.

Please visit VOWSTHCP.com for the full prescribing information and patient information.

ECOSPOR 4 was a separate open-label, single-arm study. The primary outcome evaluated the safety and tolerability of VOWST up to 24 weeks. Secondary endpoints evaluated *C. difficile* recurrence at 4, 8, 12 and 24 weeks. VOWST was used as early as first recurrence in this study. Nearly 1 out of 3 participants had a first *C. difficile* recurrence at baseline. In those participants, specifically, 94% were recurrence-free at 8 weeks, and of participants who had 2 or more recurrences at baseline, 90% were recurrence-free at 8 weeks. In the overall population, 91% were recurrence-free at 8 weeks and 86% remained recurrence-free at 24 weeks when the trial concluded. VOWST following antibiotics was generally well-tolerated in ECOSPOR 4. The most common adverse reactions were flatulence 4%, diarrhea 3%, and nausea 3%.

The VOWST manufacturing process until stringent criteria for screening donors for infectious diseases; a comprehensive ethanol purification process and filtration process. It's really an innovative approach to the manufacturing of a treatment prevent *C. difficile* recurrence.

VOWST is orally administered and can be taken by patients in the comfort of their own home; they don't need to come to the office for an invasive procedure. And from my own experience, taking it home is a fairly straightforward process for my patients. We don't get a lot of phone calls from patients about how to take it.

There is a 2-step process for the treatment. In Step 1, the patient takes a full course of antibiotics. This must be followed by a laxative to remove residual antibiotics from the GI tract. Step 2; The following day, after taking the laxative, patients take 4 capsules of VOWST, once-daily, on an empty stomach for 3 days.

Adding VOWST to my practice has allowed me to expand my options for helping my patients prevent *C. difficile* recurrence. We've taken advantage of some of the provider and patient support services available through the VOWST Voyage Program, which has helped some of my eligible patients get access.

In my opinion, the introduction of VOWST is truly game-changing for the prevention of *C. difficile* recurrences. It's an encapsulated product offering at home oral administration that is taken following antibiotics to address both phases of *C. difficile* bacteria. It's been proven superior to antibiotics alone, and has delivered durable results. Having an option like this may help recurrent *C. difficile* patients from experiencing a future recurrence.

Thank you very much for joining me today.

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ReachMD Announcer:
This Medical Industry Feature was sponsored by Nestle Health Sciences. If you missed any part of this discussion, visit *Industry Features* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!