



Potential new active substance formulation to help patients with cystic fibrosis

Deep into the lungs

Cystic fibrosis sufferers depend on drugs, physiotherapy and inhalations throughout their lives. This genetic disorder reduces lung function and makes the airways susceptible to bacterial infections. Researchers at Bayer HealthCare are developing a new treatment: Ciprofloxacin Inhale, an innovative formulation of the tried and tested antimicrobial ciprofloxacin for inhalation which combats the bacterial pathogens and is easy to use even for young patients.

Diagnosis of cystic fibrosis usually comes as a complete bombshell to new parents; after all, babies with the hereditary disorder will need special medical treatment for the rest of their lives. About 70,000 patients around the world suffer from cystic fibrosis. Mainly Caucasian people from Europe, North America and Australia are affected; researchers are unable to agree on why this genetic metabolic disorder occurs much more rarely in Asia and Africa. While sufferers' life expectancy was just

under 20 years in the past, "because of the improved treatments available, many are now able to celebrate their 50th birthday," says Dr. Barbara Hampel, Global Clinical Leader Antimicrobials at Bayer HealthCare in Berlin. A genetic defect on the long arm of chromosome 7 causes this disease, which is still incurable and varies in severity between patients, "depending on exactly where the gene is damaged," she explains. Hampel is leading the clinical development of Ciprofloxacin

Inhale (BAY Q3939), a new formulation of the tried and tested broad-spectrum antibiotic ciprofloxacin which was first licensed in 1987. Cystic fibrosis patients will inhale the active substance which will reduce undesirable colonies of bacteria in the lungs. This, in turn, will reduce the normal inflammatory processes, allowing secretions to drain away more effectively.

This is the most important thing for cystic fibrosis patients, as their genetic defect means that the chlo-



Combating cystic fibrosis: young patients are particularly hard hit by the hereditary disease (photo left). Dr. Artur Lutfullin and Dr. René Rämisch (photo above, left to right) hope that their new mini-inhaler will make treatment simpler for children and adolescents.

ride channels in the cells do not work properly and the salt/water balance is disrupted. The result of this is that various glands – especially in the lungs and the pancreas – produce mucus that is too viscous. In the lungs, this prevents the cilia from functioning properly and the thick, sticky secretion cannot be simply coughed up. “Actual lumps are formed,” says the Bayer researcher. In fact, the mucus forms the ideal breeding ground for bacteria in the airways. “About 95 percent of patients have chronic infections, which leads to chronic inflammation of the bronchi,” says Dr. Doris Staab from the Charité hospital in Berlin (see “Interview”). “It is rarely possible to eliminate the pathogens quickly,” says Hampel, “but thanks to standard treatments with antibiotics such as ciprofloxacin, we can reduce the bacterial count and so reduce the number of acute episodes of infection and lessen their severity.”

Up to now, doctors have given the Bayer antibiotic orally or intravenously. The active substance reaches its intended site of action via the bloodstream, but is also distributed throughout the body. The Bayer researchers wanted to avoid this incidental effect and develop a new system whereby the drug would be carried specifically to where it was needed. “The question was, how do we get the ciprofloxacin molecules into the lungs?” recalls Dr. René Rämisch, Global Project Leader

at Bayer HealthCare in Wuppertal. A solution was soon found: a mini-inhaler developed by a cooperation partner of Bayer HealthCare. Experts call the small device a dry powder inhaler. A capsule containing the active substance ciprofloxacin in powder form, together with a few other substances, is placed in the inhaler. Inside the plastic device, a needle pierces the capsule. The patient then places the mouthpiece between his or her lips and presses the button to release a spindle. This propels a mixture of air and active substance deep into the lungs of the cystic fibrosis sufferer.

Mini-inhaler makes for easier treatment

“The device is convenient, easy to use, does not need cleaning and is particularly suitable for teenagers who often find it embarrassing to have to take medication when they are away from home,” says Rämisch.

Many studies have confirmed that conventional ciprofloxacin formulations help in various indications such as chronic bronchitis and urinary tract infections, and also kill disease pathogens. A Phase II study is currently being held to test the efficacy of the new inhalation therapy. Children and adolescents will also be included in future studies. The researchers’ great hope is that the mini-inhaler will make treatment easier, especially for young cystic fibrosis patients.

Interview



“Growing up healthier”

Dr. Doris Staab is head of the cystic fibrosis out-patient clinic at the Pediatric Department specializing in pneumology and immunology at the Charité hospital in Berlin. *research* spoke to her about the new formulation, Ciprofloxacin Inhale.

What treatment options are there for the symptoms of cystic fibrosis?

They are based on a three-pronged attack: firstly, the patients’ missing pancreatic enzymes are replaced and they are given a high-calorie diet. Physiotherapy and sport act as the second prong of the attack. Endurance training is optimal, twice or three times a week if possible. In physiotherapy, patients learn special breathing techniques to get rid of the mucus and keep their rib cage flexible. The third line of attack is anti-infective treatment.

What have been the results so far in clinical studies with Ciprofloxacin Inhale?

Children, adolescents and adults with cystic fibrosis have tolerated the inhaled ciprofloxacin active substance well at various doses in Phase I studies. An international Phase II study is currently ongoing to test the safety and efficacy of Ciprofloxacin Inhale.

Why would children and adolescents in particular benefit from the new formulation?

Although it will not spare them the unpleasant and painful intravenous therapy in hospital entirely, it could mean that it is required less often. Daily inhalation with a nebulizer, which takes time both for the nebulization and for cleaning the device, is avoided. And if they are treated early with regular antibiotic inhalation, chronic Pseudomonas infections may not occur until later, allowing children to grow up healthier.

➔ www.cff.org
The Cystic Fibrosis Foundation website contains information on the disease, treatment options and has offerings for sufferers, doctors, health care professionals and scientists.