1. SUMMARY

TITLE

An open, multicenter, long-term study to assess the efficacy and tolerance of Kreon® in patients with pancreatic exocrine insufficiency caused by cystic fibrosis in comparison with a historical control group of healthy children.

INVESTIGATORS

Removed for privacy reasons

STUDY DESIGN

This was an open, multicenter (two study centers) long-term study in children with pancreatic exocrine insufficiency due to cystic fibrosis in comparison with a historical control of healthy children. The duration of treatment within this study was planned to be two years with visits repeated at six-monthly intervals.

AIMS

The aim of this study was to assess half-yearly the efficacy and tolerance of Kreon® on selected objective and subjective parameters in a cystic fibrosis population compared with a historical control group of healthy children according to Oehmich (1) (standard values of physical (somatic) development of healthy children). Actually, the children's heights and body weights were compared to the percentile curves of healthy children published by Kunze (1977) (2).
METHODS

After an initial visit treatment with Kreon® started and the patients had to return to the clinic every six months. At these regular visits, body weight, height, FVC, FEV₁, the Shwachman Score, the number of days of hospitalization and the number of days during which chemotherapeutics had to be taken for respiratory tract diseases during the past 6 months were recorded as well as concomitant medications and adverse events. Furthermore, blood was drawn from the patients in order to determine laboratory parameters.

DRUGS AND DOSAGES

Kreon® is a pancreatin preparation containing 300 mg of pancreatin with a declared enzyme value of 8000 Ph.Eur. units lipase, 9000 Ph.Eur. units amylase and 450 Ph.Eur. units protease.

4-15 capsules should be taken daily. Changes of the dosage had to be documented in the CRFs together with the reason for change.

PATIENTS ENTERED

A total of 29 patients entered this study, 15 in the center of Dr. Henker, Dresden, Germany (Center 1) and 14 in the center of Prof. Hein and Dr. Breuel in Rostock, Germany (Center 2). All patients completed the two-year study.

PATIENT CHARACTERISTICS

Fifteen patients (52%) were male and 14 patients (48%) were female. Mean age of the patients was 10 years (range 3 - 14 years) with the mean duration of cystic fibrosis being 8.4 years. Body weight upon entry into the study ranged between 14 and 45 kg with an average of 27 kg. A total of 27 patients (93%) had a height/body weight relationship below the median as compared to the percentile curves of healthy children published by Kunze (1977).

RESULTS

Efficacy

Both, body weight and height in the median increased continuously over the two-year observation period with a median increase of 5.2 kg body weight and 10.5 cm height at the end of the study.

The age/height and height/body weight relationships were compared to the percentile curves of healthy children according to Kunze (2) and categorized into seven categories. Most
patients maintained the category or even improved during the two years of treatment with
Kreon®. Only three worsened during the study course.

FVC on the average increased slightly but continuously over the entire treatment period.

The Shwachman Scores on the average remained almost unchanged throughout the study.

The majority of patients (22, 76%) were not hospitalized during the course of this study. A total
of 22 patients (76%) needed chemotherapy (antibiotics) for the treatment of respiratory tract
diseases at least once during the study.

Safety data

Adverse events were documented for a total of 14 patients (48%), none of which was
considered by the investigators to be related to Kreon® treatment. The most frequently
reported adverse events were related to the respiratory system (10 patients, 34%) and to the
body as a whole (8 patients, 28%), with the most frequent adverse events being infection (7
patients, 24%) and fever (5 patients, 17%).

Pulmonary exacerbation in 3 patients and hemoptysis in one patient were considered to be
serious adverse events, as the patients had to be hospitalized due to the events.

Laboratory measurements were only performed for a few patients, so that no summary was
generated.

CONCLUSION

The physical development of the majority of cystic fibrosis patients (79%) was age-appropriate
and increased steadily during a two years treatment period with Kreon®.

Only 3 hospitalizations due to serious adverse events (disease related pulmonary problems)
were necessary during this study. Four additional ones were preplanned.

The safety data revealed that longterm therapy with Kreon® is very well tolerated.