Safety and Efficacy of Inhaled Human Alpha-1 Antitrypsin (AAT) in Cystic Fibrosis (CF): a Phase II Clinical Study

Eitan Kerem[1], Shabtai Bauer[2], Pnina Strauss[2] , Nicole Jaffe[2], Shoshana Armoni[1], Thea Pugatsch[1], David Shoseyov[1] ,Naveh Tov[2]

[1]Department of Pediatrics and CF Center, Hadassah Hebrew University Medical Center, Mt. Scopus, Jerusalem, Israel
[2]Kamada Ltd., Science Park, Ness-Ziona, Israel

Introduction

CF is characterized by recurrent and chronic infection with chronic neutrophilic inflammation, leading to progressive lung damage. Neutrophilic inflammation is associated with the release of excessive neutrophil elastase (NE) levels, which cause further damage to the respiratory tissue. The major antagonist of the proteolytic enzyme NE is AAT. In CF, the unregulated inflammatory process overwhelms the normal NE/AAT balance, leading to accumulation of NE in the lung and ultimately to tissue damage. The rational for inhaled AAT therapy is to treat this imbalance and prevent further damage to the lung tissue by preventing/reducing this destructive cycle. Recently, a high purity, liquid, ready-to-use AAT was developed (Kamada Ltd., Israel) for inhalation via a customized Investigational eFlow Nebulizer System (PARI Pharma, Germany). The aim of this phase II study was to assess the safety and efficacy of inhaled AAT in CF patients.

Study Design

Double-blind, randomized, placebo-controlled, repeated dose.

Study Method

21 patients were randomized (2:1) to receive inhaled 80mg active AAT or placebo once a day. The study comprised three treatment periods, i.e., 1 day, 7 days and 28 days. Safety and efficacy variables were tested.

Table 1: Adverse Event relation to study drug

Relation to study drug	Active: 80mg AAT (N=14)	Placebo control (N=7)
All AE's	17 (100%)	27 (100%)
Unrelated	16 (94.1%)	27 (100%)
Possible	1 (5.9%)	0 (0%)

Conclusion

Kamada AAT was safe and well tolerated when inhaled daily for 28 days. The observed reduction of neutrophils and NE in sputum suggests an anti-inflammatory role in CF patients. Further clinical trials with a larger cohort are warranted to determine clinical outcomes such as effects on exacerbation events and disease progression.

Results

All patients completed the study without SAEs. One patient reported mouth dryness, with a possible relation to the study drug. A decrease in the sputum neutrophil counts and in sputum NE levels was found in the AAT group, but not in the placebo group.

Figure 1: Sputum analysis for Neutrophil Elastase

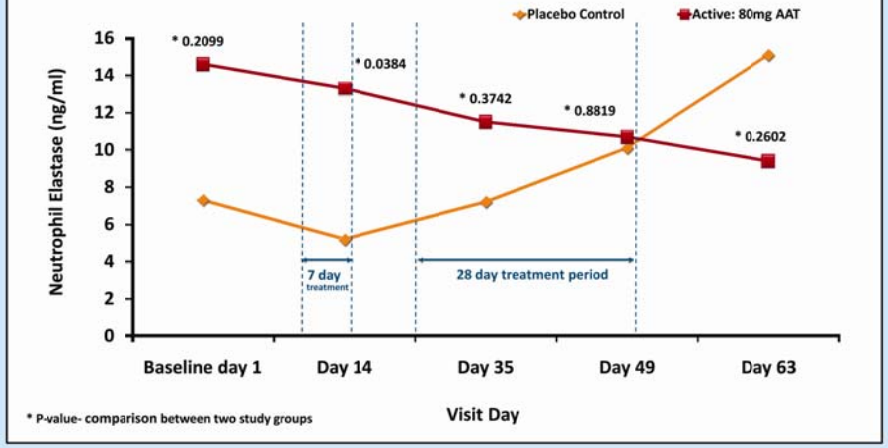

Figure 2: Sputum analysis for Neutrophil count