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Title:

KB001-A, A NOVEL ANTI-INFLAMMATORY, FOUND TO BE SAFE AND WELL TOLERATED IN CYSTIC FIBROSIS PATIENTS INFECTED WITH *PSEUDOMONAS AERUGINOSA*

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What was your research question?

Our study was done to evaluate the safety and treatment benefits of a new therapy for people with cystic fibrosis (CF), who are infected with *Pseudomonas aeruginosa*.

Why is this important?

This therapy is important as *Pseudomonas aeruginosa* (Pa) is one of the most common bacteria present in the lungs of people with CF. Chronic Pa infection is associated with inflammation and progressive loss of lung function, which are hallmarks of CF lung disease. Pa has many ways in which it is influencing the lung disease. One of these ways is by forming a complex needle-like machine on its surface called the type III secretion apparatus (TSS), which the bacteria uses to insert bad (toxic) proteins into cells. KB001-A is a novel therapy developed to attack Pa infection by targeting this mechanism Pa uses to cause disease.

What did you do?

This study evaluated KB001-A as an intravenous treatment people with CF who were 12 -50 years of age and who were infected with Pa to determine if it would change the time needed

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for their next course of antibiotics. This was a study during 16 weeks with a control group that received a placebo (a 'dummy' treatment) (a randomised, double-blind, placebo-controlled study). This study was done to evaluate the safety and effects (efficacy) of KB001-A. The drug was given at 0, 2, 4, 6 and 16 week time points. The study also assessed changes in symptoms, lung function, and signs of inflammation (inflammatory markers).

What did you find?

182 individuals were screened, 169 received at least one infusion of KB001-A (n=83) or placebo (n=86). KB001-A was generally safe and well-tolerated as compared to placebo, with no significant emergent adverse effects. Time to need for antibiotics did not differ between groups. A 3.2% increase in forced expiratory volume at one second (FEV1) from placebo favouring KB001-A was observed at week 16. Several inflammatory markers were assessed and showed significant improvement in only one marker (IL-8) with treatment.

What does this mean and reasons for caution?

The study results showed that KB001-A was safe and well-tolerated and associated with a modest FEV1 benefit and reduction in select sputum inflammatory markers (IL-8). KB001-A was not associated with a change in time to need for antibiotics. The lack of effectiveness seen with KB001-A may be due, in part, to the low levels of the type III secretion proteins that have previously been reported in sputum of people with CF chronically infected with Pa.

What's next?

This therapy in its current formulation did not prove to be beneficial in treating people with CF infected with Pa. Whether or not there are subsets of people that may benefit from this type of therapy either as an anti-infective or anti-inflammatory in the future remains to be seen.

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