

primary studies - published RCT

## **Randomised double blind placebo controlled trial investigating the effect of calcium and vitamin D supplementation on bone mineral density and bone metabolism in adult patients with cystic fibrosis.**

**Code:** PM15698940

**Year:** 2004 **Date:** 2007

**Author:** Haworth CS

### **Study design (if review, criteria of inclusion for studies)**

Randomised 1:1 in blocks of 12 stratified by centre. Double-blinding. Public funding.

### **Participants**

483 European CF patients, 2-18 years of age without *P. aeruginosa* colonization were randomly assigned to receive four intramuscular injections of a bivalent *P. aeruginosa* flagella vaccine or placebo over a 14-month period. Patients were evaluated quarterly for *P. aeruginosa*-positive throat cultures and antipseudomonal serum antibody titers during the study period of 2 years.

### **Interventions**

4 doses of vaccine consisting of pseudomonas flagella proteins of subtypes a0a1a2 and b from strains 1210 and 5142, respectively, every 4 weeks (first 3 doses) and last dose after 1 year, or placebo.

### **Outcome measures**

Another outcome was added during the trial: chronic infection, diagnosed by 3 positive swabs or titres during 1 year. Other outcomes were: specific antibodies against vaccine components and flagella subtypes; adverse events. FEV1 was measured but no data were provided. Primary: infection with *P. aeruginosa*, diagnosed by a positive throat swab or positive antibody titre towards other antigens (exotoxin A, alkaline protease, or elastase) than the flagella proteins in the vaccine.

### **Main results**

The vaccine was well tolerated, and the patients developed high and long-lasting serum anti-flagella IgG titers. In the intention-to-treat group (all patients enrolled), 82 of 239 vaccinated patients had *P. aeruginosa* infection and/or antipseudomonal serum titers compared with 105 of 244 patients in the placebo group ( $P = 0.05$ ; relative risk: 0.80; 95% CI: 0.64-1.00). Analysis of the 381 patients in the per-protocol group, who received all four vaccinations or placebo treatments, revealed 37 of 189 patients with infection episodes in the vaccine group compared with 59 of 192 patients with such episodes in the placebo group ( $P = 0.02$ ; relative risk: 0.66; 95% CI: 0.46-0.93). *P. aeruginosa* strains, exhibiting flagella subtypes included in the vaccine, were significantly less frequently isolated from vaccinees than from placebo controls ( $P = 0.016$ , relative risk: 0.319; 95% CI: 0.12-0.86).

### **Authors' conclusions**

Chronic *P. aeruginosa* infection was rare because of recent institution of early antibiotic eradication regimes. Active immunization of patients with cystic fibrosis lowers the risk for infection with *P. aeruginosa* and therefore may contribute to a longer survival of these patients.

<http://dx.doi.org/10.1016/j.jcf.2004.08.002>

### **See also**

J Cyst Fibros. 2004 Dec;3(4):233-6.

### **Keywords**

Adolescent; Bacterial Infections; Child; Immunization; Infection; pharmacological\_intervention; placebo; Pseudomonas aeruginosa; Pseudomonas; Pseudomonas Vaccines; Respiratory Tract Diseases; Respiratory Tract Infections;