primary studies - published RCT

A double-blind randomized placebo-controlled phase III study of a Pseudomonas aeruginosa flagella vaccine in cystic fibrosis patients.

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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 antiflagella 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 vaccinates 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.

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See also

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Keywords

Adolescent; Bacterial Infections; Child; Immunization; Infection; pharmacological_intervention; placebo; Pseudomonas aeruginosa; Pseudomonas; Pseudomonas Vaccines; Respiratory Tract Diseases; Respiratory Tract Infections;