primary studies - published RCT

RAD in stable lung and heart/lung transplant recipients: safety, tolerability, pharmacokinetics, and impact of cystic fibrosis.

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

Phase I, multicenter, randomized, double-blind, two-period, two-sequence, crossover study.

Participants

Of the 20 patients randomized, 8 had CF and 12 did not.

Interventions

Single doses of RAD capsules at doses of 0.035 mg/kg (2.5 mg maximum) or 0.10 mg/kg (7.5 mg maximum) were administered with cyclosporine (Neoral [cyclosporine, USP] modified), steroids, and azathioprine on Day 1. The alternate dose was administered on Day 16.

Outcome measures

Laboratory assessments, vital signs, and adverse events were recorded throughout the study. RAD pharmacokinetic profiles were assessed over a 7-day period following each dose. Steady-state cyclosporine (CsA) profiles were assessed at baseline and with each RAD dose; RAD and CsA trough concentrations were obtained throughout the study period.

Main results

Single doses of RAD were safe and well tolerated. Headache was the most common side effect. RAD produced a mild, dose-dependent, reversible decrease in platelet and leukocyte counts. Cholesterol and triglycerides were minimally affected. At both doses, CF patients had significantly lower peak concentrations of RAD than did non-CF patients ($p = 0.03$); however, overall exposure (area under the curve/dose) was not different between the groups ($p = 0.63$). At the higher dose, there was a clinically minor under-proportionality in AUC, averaging -11%. Steady-state pharmacokinetics of CsA were not affected by RAD co-administration.RAD was safe and well tolerated by stable lung and heart/lung transplant recipients with and without CF.

Authors' conclusions

The presence of CF did not influence the extent of RAD exposure. Single doses of RAD did not affect the pharmacokinetics of CsA. Ongoing studies are assessing the long-term safety and efficacy of RAD in lung and heart/lung transplantation.

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See also

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Keywords

Adolescent; Adult; Anti-Bacterial Agents; Cyclosporin; Heart-Lung Transplantation; Immunosuppressive Agents; Lung Transplantation; Macrolides; non pharmacological intervention - surg; pharmacological_intervention; transplantation; Bacterial Infections; Respiratory Tract Infections; Respiratory Tract Diseases; Infection; Capsules; Azathioprine; Steroids;