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Beneficial Effects of Simvastatin and Pravastatin on Cardiac Allograft Rejection and Survival

In their study comparing beneficial effects of simvastatin and pravastatin on cardiac allograft rejection and survival, Mehra et al. (1) concluded both statins to be equivalent and superior to no-statin treatment. Clinical trials whose purpose are to show equivalence/noninferiority of two or more treatments commonly apply methods to demonstrate superiority and, if no statistical differences are found, treatments are assumed to be equivalent. The correct approach, however, would be to calculate sample sizes using bio-equivalence formulae (2). Although the findings of the statin trial are reassuring, the study could have been underpowered. Could the investigators comment on power-size calculation prior to this study and whether the concept of equivalence testing was adhered to?

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REPLY

I am grateful to Dr. Conraads for the opportunity to respond to the issues raised and am pleased to note that our findings provide reassurance to our colleague in the comparative usefulness of either simvastatin or pravastatin following cardiac transplantation. Ever since the original publication by Kobashigawa et al. (1), wherein the beneficial immunomodulating properties of pravastatin on indices of cardiac allograft rejection were reported, it has remained an enigma whether other drugs within the class share this property. Assuming a 25% incidence of allograft rejection requiring treatment at one year, given the cohort size, the current study had 80% power to detect a 15% difference in rejection rates between either pravastatin or simvastatin, with a type-1 error of 0.05. Thus, based on our results, it is unlikely that pravastatin is superior to simvastatin in abrogating cardiac allograft rejection.

Insofar as the issue of survival is concerned, we agree that the study could have been underpowered as a single-center experience is unlikely to enroll the requisite number of transplants that would be required to confirm or refute a difference in survival alone. Nevertheless, we must emphasize that the survival rates in our study (92% and 91% for pravastatin and simvastatin, respectively) are in agreement with those previously reported by other single-center studies (95%) of statins (1) and superior to those reported by multicenter registry databases (83%) that have a relatively low penetration of statin use (2). Because allograft rejection is the prime driver of survival in the first year, we strongly believe that our study should restore confidence in the similar safety and efficacy of low-dose statin therapy and steer us toward a more universal use of these agents to enhance outcomes in cardiac transplantation.

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