Applying propensity methods to the United States transplant registry for external real-world evidence control arms for 5-year survival in the BENEFIT study

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Abstract

To address the challenges of assessing the impact of a reasonably likely surrogate endpoint on long-term graft survival in prospective kidney transplant clinical trials, the Transplant Therapeutics Consortium established a real-world evidence workgroup evaluating the scientific value of using transplant registry data as an external control to supplement the internal control group. The United Network for Organ Sharing retrospectively simulated the use of several distinct contemporaneous external control groups, applied multiple cause inference methods, and compared treatment effects to those observed in the BENEFIT study. Applying BENEFIT study enrollment criteria produced a smaller historical cyclosporine control arm (n = 153) and a larger, alternative (tacrolimus) historical control arm (n = 1069). Following covariate-balanced propensity scoring, Kaplan-Meier 5-year all-cause graft survivals were 81.3% and 81.7% in the Organ Procurement and Transplantation Network (OPTN) tacrolimus and cyclosporine external control arms, similar to 80.3% observed in the BENEFIT cyclosporine treatment arm. Five-year graft survival in the belatacept-less intensive arm was significantly higher than the OPTN controls using propensity scoring for comparing cyclosporine and tacrolimus. Propensity weighting using OPTN controls closely mirrored the BENEFIT study's long-term control (cyclosporine) arm's survival rate and the less intensive arm's treatment effect (significantly higher survival vs control). This study supports the feasibility and validity of using supplemental external registry controls for long-term survival in kidney transplant clinical trials.
To read the entirety of the manuscript, view it in its original format in the *American Journal of Transplantation* here. (Subscription to *AJT* required).