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Progress in Kidney Xenotransplantation: Are We Ready for Clinics?

JAESEOK YANG
Severance Hospital, Republic of Korea

Organ shortage is the most important hurdle in the field of transplantation and xenotransplantation is a promising alternative to solve this problem. Recent remarkable development of gene editing technology has improved generation of multiple genetically-modified pigs for xenotransplantation and subsequent outcomes of xenotransplantation. Thanks to this achievement, solid organ xenotransplantation has been performed in human decendent models and finally in patients as clinical trials. For successful xenotransplantation, establishment of effective and safe systemic immunosuppressive regimens is also important. Depletion of T and B cells are needed as an induction therapy. Costimulatory blockade such as anti-CD40L, anti-CD40, CTLA-4Ig, anti-CD28, and anti-ICAM-1, is an essential component of immunosuppressive regimens. Inhibitors of pro-inflammatory cytokines, such as TNF-α, IL-1bβ, and IL-6 could be supplemental. Furthermore, complement inhibitors are needed to suppress vigorous activation of complements in xenotransplantation. Oral immunosuppressants, such as prednisolone, tacrolimus, mycophenolate mofetil, and mTOR inhibitors are also needed as a maintenance therapy. Optimal combinations of various categories of immunosuppressants are now under investigation for further application to clinical trials.

Keywords: Xenotransplantation, Genetically-modified pig, Immunosuppression, Clinical trial, Organ shortage