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## **Tolerance Induction in Kidney Transplantation with Combined Bone Marrow Transplantation**

**Jae Berm Park**

*Samsung Medical Center, Republic of Korea*

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Many advances have been made in kidney transplantation over the past two to three decades. Nevertheless, progress in improving long-term graft outcomes has been very limited. Ironically, the long-term maintenance of immunosuppression has been well recognized as a limitation to long-term graft improvement due to its complications. Therefore, the induction of immune tolerance, to maintain stable renal graft function without the need for immunosuppressive drugs, is still the ideal condition after renal transplantation. The concept of tolerance induction aims to reprogram the recipient's immune system to accept the transplanted kidney as a part of their own body, thereby maintaining stable graft function without immunosuppression. Various strategies had been proposed for tolerance induction in organ transplantation. Among these, chimerism through the bone marrow or hematopoietic stem cell transplantation has emerged as the potential way to tolerance induction, which based on the various researches including experiments in primate models, and clinical investigations. As part of this ongoing endeavor, our institute has undertaken primate experiments and clinical studies focused on achieving transient chimerism and inducing immune tolerance through combined kidney and bone marrow transplantation (CKBMT) in living kidney transplant patients. Our recent protocol for tolerance induction within CKBMT incorporates a conditioning regimen involving cyclophosphamide, fludarabine, and thymic irradiation, coupled with induction therapy utilizing rituximab and anti-thymocyte globulin (rATG). Tacrolimus and steroids are employed for the maintenance of immunosuppression (IS) in the early post-transplantation. From our experiences, the conditioning and immune suppression regimens had been modified and was reported. Our recent protocol has demonstrated the successful achievement of transient chimerism and maintenance of sustained graft function without the need for continuous immunosuppression. Tolerance induction trials continue to evolve, with ongoing research geared at refining protocols and gaining a deeper understanding of the complex mechanisms underlying this revolutionary approach to renal transplantation.