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## **Optimal Maintenance Immunosuppression Regimen for Long Term Allograft Outcome**

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Currently, a so-called standard maintenance immunosuppressive regimen in kidney transplantation includes calcineurin inhibitors (CNIs), mycophenolate, +/- corticosteroids. CNIs are critical components of maintenance immunosuppressive regimens. The use of CNIs resulted in significant improvements in early allograft survival by reducing the incidence of acute rejection. However, there has been no significant improvement in long-term allograft survival, owing primarily to long-term complications of immunosuppression. Patient death due to cardiovascular complications, infections, or malignancies still the main problem of long-term graft loss. Moreover, chronic CNI nephrotoxicity is thought to have substantial effects on the kidney allograft. To address the issue of CNI nephrotoxicity and its long-term negative consequences, several immunosuppressive regimens that avoid, eliminate, or minimize CNIs are being investigated. Avoiding CNIs and instead using a mammalian target of rapamycin (mTOR) inhibitor or belatacept appears to increase the risk of acute allograft rejection. However, using fusion protein results in comparable graft to that of CNIs in long-term. CNI elimination with mTOR or mycophenolate replacement may be necessary in certain patients with certain malignancies, such as Kaposi sarcoma, or non-melanoma skin cancer. CNI minimization is a widely used strategy for reducing CNI exposure. When recommended levels of CNI have been achieved, it is possible to combine mycophenolate or mTOR inhibitor with a reduction in CNI. However, the combination of mTOR inhibitor with CNI may result in a reduction in CNIs to lower levels compared to those used in combination with mycophenolate. In conclusion, three-drug maintenance immunosuppression regimen is a standard strategy used in kidney transplantation. It includes CNI, mycophenolate or mTOR inhibitor, +/- corticosteroids. Belatacept shows promise as an alternative for CNI. Despite a lack of sufficient data on the optimal immunosuppressive regimen, personalized immunosuppression appears to be the most effective strategy for enhancing the long-term

survival of both patients and kidney allografts

**Keywords:** Calcineurin inhibitors, Personalized immunosuppression, CTLA-4, mTOR inhibitors, Allograft survival