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Do we need Certican to improve long-term graft and patient outcome in kidney transplantation?

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Analysis using data from registries has confirmed that the risk of de novo malignancies is increased in transplant recipients, with a relative risk 3–5 times that of the general population. Malignancy has become the main cause of death post-transplantation according to ANZDATA registry 2014 report.
Another study using a national health insurance database in Korea reaffirmed a higher risk of malignancy among KT recipients for 14 of 29 cancer types, most of which were diagnosed earlier than the control group. CNI-associated nephrotoxicity occurs early after transplant and progresses over time.
Data have demonstrated that lowering CNI dose can reduce CNI nephrotoxicity; therefore, it has been proposed that the duration of CNI therapy should be limited. Tacrolimus and cyclosporin can increase production of transforming growth factor β1 (TGFβ1) in tumor cells, leading to increased tumor growth. Cyclosporin can also increase expression of vascular endothelial growth factor (VEGF), leading to increasing angiogenesis for tumor growth, and has been reported to increase IL-6 production in B cells, leading to B cell activation and proliferation and thus increasing the risk of posttransplant lymphoproliferative disorder (PTLD) development. Furthermore, cyclosporin can directly impair DNA repair in kidney transplant recipients. In vitro and in vivo studies have demonstrated activation of the oncogenic RAS–RAF pathway by calcineurin inhibitors, contributing to renal cell carcinoma (RCC) growth. In a retrospective analysis using registry data of renal transplant patients, there was a reduced incidence of de novo malignancies with mTORi-containing regimens compared with those that contained CNIs. TRANSFORM study demonstrated that Occurrence of benign or malignant neoplasms was numerically lower in everolimus plus low CNI arm compared with mycophenolate plus standard CNI at 24 months.
mTOR inhibitors, although immunosuppressive agents, may contribute to a lower risk of CMV-induced disease by inhibiting the mTOR pathway. mTOR treatment, during the effector to memory transition phase enhances the memory differentiation program resulting in a significantly higher number of virus specific memory CD8+ T cells. CMV-specific CD4+ T cells of EVR treated patients have shown strong functionality which may confer protection

against CMV infection. Inhibition of mTOR may also regulate the inflammatory response providing protection against the viral infection.
mTOR pathway plays a critical role in replication of BKV in host cell. A lower incidence of BKVN was observed following mTORi-based regimens compared with TAC, MMF or non-mTORi regimens. There was a reduced incidence of BKV with the EVR+rCsA/rTAC compared to the MPA+sCsA/sTAC.