

Transplant Immunology II

De novo use of mTOR inhibitors in solid organ transplantation

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De novo use of mTOR inhibitors with CNI minimization has to be differentiated from delayed/rescue use in combination with CNI elimination/replacement. The presented data will focus on the concept of de novo use in combination with CNI minimization.

Large phase III trials in kidney, liver, heart and lung transplantation have consistently demonstrated the efficacy of this concept with significant advantages, such as reduction of CMV infections, reduction of BKV infections particularly in renal transplant patients, improvement of renal function in liver transplant recipients and particularly reduction of graft arteriosclerosis in heart transplant recipients.

The presence of minimized CNI additionally demonstrated almost abrogation of dnDSA or non-DSA development, typically observed in conversion studies with CNI elimination. Particular side effects such as wound healing problems, incisional hernias, and lymphoceles, typical for combinations of two proliferation inhibitors such as MMF/MPA and mTOR as demonstrated in the CNI elimination studies with mTOR replacement, were similar between study arms, as well as proteinuria as a typical side effect in rescue studies, where mTORI were considered as replacement for CNI induced nephrotoxicity. Most interestingly did all studies indicate a reduced de novo incidence of malignancies, as well as reduced recurrence rates of HHC in liver transplant recipients.