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LEUCOPENIA AFTER KIDNEY TRANSPLANTATION: SWITCHING MYCOPHENOLATE TO MTOR INHIBITOR APPEARS SAFE AND FEASIBLE TO REDUCE THE RISK OF ALLOSENSITIZATION

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Background and Aims: Mycophenolate acid (MPA) is a standard component of maintenance immunosuppression after kidney transplantation. MPA, however, increases the risk of leucopenia. In the past, mTOR inhibitors (mTOR-I) in combination with calcineurin inhibitors (CNI), were considered immunologically safe but showed higher mortality in the long term.

Method: We conducted a retrospective single-center study analyzing 98 kidney transplant recipients (KTRs) under standard triple maintenance immunosuppression between 2020 and 2022 who developed leucopenia. We compared patient and kidney allograft outcomes between 31 KTRs who were temporarily switched from MPA to mTOR-I and 67 KTRs who underwent a reduction of MPA dose.

Results: A switch to mTOR-I was performed more often in case of a CMV high-risk status (50% vs. 21%, $p = 0.009$), CMV primary infection (68.2% *vs.* 22%, $p<0.001$), and more severe leucopenia (median nadir of neutropenia: 0.52 G/L vs. 0.86 G/L, $p = 0.023$). The median duration of leucopenia was comparable between the two groups (69 vs. 80 days). 9 of 67 KTRs (13%) developed *de novo* donor-specific antibodies *(dn*DSA) under reduced MPA compared to 1 of 31 KTRs (3%) under mTOR-I ($p = 0.17$). Biopsy-proven rejections were comparable between the two groups (1 in each). There was a slight but insignificant improvement of eGFR under mTOR-I compared to MPA (ΔeGFR +17 vs. +7 ml/min/1.73m2, $p = 0.13$) and no difference in proteinuria.

Conclusion: A temporary switch from MPA to mTOR-I is a feasible and safe strategy to overcome leucopenia, especially in cases of CMV high-risk status and CMV primary infection. No significant adverse effects on kidney allograft outcomes were observed. Development of dnDSA tended to be lower in the mTOR-I group, suggesting that this strategy may have the potential to reduce the risk of allosensitization.