INTRODUCTION AND AIMS: Mesenchymal stromal cells (MSC) are currently being assessed in kidney transplantation (KTx) as an alternative strategy for tolerance induction and/or graft rejection (AR) prevention/treatment. The present prospective phase I-II trial reports on the 1-year follow-up of the first use of third-party allogeneic MSC in deceased donor kidney transplant recipients (KTR) under standard immunosuppression.

METHODS: On postoperative day 3±2, 10 KTR received a single injection of third-party MSC (~2.9x10^6/kg BW), in addition to standard immunosuppression regimen (Basiliximab induction, Tacrolimus, Mycophenolate Mofetil and Steroids), and were compared to 10 concomitant KTR and to our whole KTR cohort transplanted throughout the study recruiting period. All included KTR were aged between 18 and 75 years and underwent first successful KTx from a cadaveric organ donor. KTR were considered ineligible for enrollment if they had a past history of malignant disease, active uncontrolled infection, EBV-negative status, panel reactive antibodies > 50% or cardiovascular instability post KTx. MSC were not matched with kidney recipient or donor’s HLA. Primary endpoint concerns safety issues of MSC infusion after KTx. Secondary endpoints were defined as the impact of MSC on graft outcomes and immunity, as well as the occurrence of anti-MSC donor HLA antibodies. Glomerular filtration rate (eGFR) was estimated using MDRD equation. Anti-HLA detection and identification were done by Luminex solid phase antibody detection technology. Lymphocyte phenotyping was performed using flow-cytometry. Regulatory T cells (Tregs) were defined as CD4^+ CD25^+ FoxP3^+ lymphocytes.

RESULTS: No hemodynamic or immune-allergic side-effect was noted at the time of MSC injection. One patient had a non-ST-elevation myocardial infarction (NSTAMI) ~3h after MSC infusion. All patients and grafts in MSC group survived during the 1-year follow-up. Still, at day 286 post KTx, one MSC-treated patient required temporary hemodialysis in a context of sepsis, type B aortic dissection and STEMI. Incidences of opportunistic infections and AR were comparable among groups. At D7, eGFR in MSC-treated KTR reached 48.6 ml/min, compared to 32.5 ml/min in matched KTR (p=0.07) and 29.3 ml/min in the cohort (p=0.01). No difference was observed among groups in 90-day eGFR slopes or eGFR levels at 1 year. MSC-treated KTR showed increased frequencies of Tregs at D30 in comparison to concomitant controls. Four patients developed antibodies against MSC or shared kidney-MSC HLA, with only 1 reaching mean fluorescence intensity >1500.

CONCLUSIONS: No safety signals were reported following a single infusion of allogeneic MSC at the time of KTx, except one questionable cardiac event. MSC therapy is associated with increased Treg proportion among CD4^+ cells and improved early allograft function. Long-term effects, including potential immunization against MSC, remain to be studied.