Conclusions: ARA 290 protected pancreatic islets from cytokine-induced damage and apoptosis *in vitro* and ameliorated the inflammatory response following PITx. It appears to be a promising candidate for improvement of PITx.

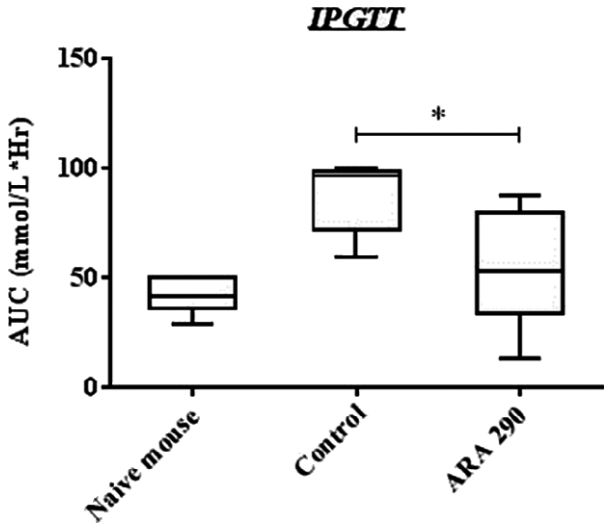

Figure1: AUC in IPGTT is compared among naïve mouse, PITx with PBS (control) and PITX with ARA290 (ARA 290). (*$p < 0.05$ versus control group; values are depicted as lower quartile, median and upper quartile (boxes) with minimum and maximum ranges.).

BO275 VASCULAR SEQUESTRATION OF DONOR-SPECIFIC ANTIBODIES PROTECTS ALLOGENEIC ISLETS FROM HUMORAL REJECTION

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Introduction: Islets grafting restores endogenous insulin production in Brittle type 1 diabetic patients, but long-term outcomes remain disappointing due to destruction of allogeneic islets by recipients' adaptive immune system. In solid organ transplantation, antibody-mediated rejection (AMR) is recognized as the first cause of transplant failure. This experimental murine study aimed at determining whether donor-specific antibodies (DSA) also contribute to islet grafts destruction.
Methods and results: Diabetes was induced by streptozotocine injection in RAG2 KO C57BL/6 (H-2^b) mice, which lack T and B cells. Allogeneic (CBA, H-2^k) islets were not rejected by these immunocompromised recipients, which remained euglycemic until the end of the follow-up (120 days). DSA (either polyclonal immune sera or murine IgG2a anti H-2k mAb) were able to bind to CBA islets and induce complement-dependent destruction β cell line *in vitro*. In contrast, repeated IV injections of DSA did not impact CBA islet grafts function *in vivo*. Live imaging studies, using radiolabelled DSA, showed that alloantibodies were sequestrated in recipients' vascular bed. As a consequence DSA that were able to bind to allogeneic endothelium of CBA heart transplant, failed to reach CBA islets. Indeed, while the vascularisation of transplanted organs comes from the donor, graft vascularisation develops from recipient and is therefore not allogeneic.
Conclusion: Our study demonstrates that, in contrast with solid organ transplants, islet grafts are protected from humoral rejection due to vascular sequestration of DSA.

BO276* ROLE OF BONE MARROW-DERIVED STEM CELLS, RENAL PROGENATOR CELLS AND STEM CELL FACTOR IN CHRONIC RENAL ALLOGRAFT NEPHROPATHY

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Background: Bone marrow-derived stem cells (BMSCs) the hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs) are pluripotent cells that can be mobilized into circulation and recruited to sites of inflammation. The present work was designed to study circulating HSCs,MSCs and renal progenitor cells (RPCs) and stem cell factor (SCF) in patients with chronic allograft nephropathy (CAN) in relation to renal hemodynamics and histopathological changes.
Subjects: This study included 45 subjects, they were divided into three groups each 15, renal transplant patients with stable renal function (Group I), with CAN (Group II) and healthy subjects as controls (Group (III).
Methods: The HSCs and MSCs were identified as CD34 + CD45 + CD117 + and CD34−CD45−CD106+ cells using flow cytometry. Serum SCF levels were measured using enzyme linked immunosorbant assay kit. C-reactive protein (CRP),urinary alkaline phoshatase (U.ALP) were measured. Immunohistochemical staining of renal biopsy was done using monoclonal antibodies against CD133 for detection of CD133 + RPCs, CD34 for detection of CD34 + stem cells,vascular endothelial growth factor (VEGF) as vascular marker and alpha smooth muscle actin (a-SMA) for renal fibrosis. Renal hemodynamics was evaluated by duplex Doppler and resistive and pulsatility indices (RI, PI) were calculated.
Results: There was a significant increase in the level of SCF,number of HSCs,MSCs,RI and PI with a decrease of U. ALP in transplanted patients than the controls. These were positively correlaed with each other and with the markers of renal function. The renal CD133 + and CD34 + cells were positively correlated with each other and with VEGF and negatively with ASMA and fibrosis.
Conclusion: Renal transplantation is assocated with mobilization of BMSCs from the BM into the circulation in parallel with an increased production of SCF with severe kidney injury. The activation of endogenous RPCs may play a role in limiting renal fibrosis and enhancing renal vasculature.

BO277 WHARTON'S JELLY MESENCHYMAL STEM CELLS AMELIORATE CISPLATIN-INDUCED ACUTE KIDNEY INJURY IN MICE

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Background/Aims: Acute kidney injury (AKI) remains a common clinical problem with high mortality rates. Mesenchymal stem cells were so far shown as a promising treatment option. It was recently reported that human Wharton's jelly derived mesenchymal stem cells (WJ-MSC) could ameliorate renal function induced by low dose of cisplatin in rats. However, the role of WJ-MSC in AKI induced with high nephrotoxic dosage cisplatin protocol (comparable to human chemotherapeutic scheme) has not yet been demonstrated. Therefore, we tested whether administration of multipotent WJ-MSC to mice with cisplatin-induced AKI (17 mg/kg body weight intraperitoneally) could improve kidney function and ameliorate damage in the kidney (the outcome through amelioration of apoptosis and induction of tubular proliferative response). The distribution of transplanted stem cells after peripheral infusion was also assessed.
Methods: WJ-MSC were injected intravenously, 24 h after cisplatin application. Cells were labeled with DiI for ex vivo tracing. At 96 h after cisplatin induced AKI, serum creatinine and blood urea nitrogen were measured and renal morphology analysis was assessed by histology to confirm the renoprotective effects of transplanted WJ-MSC. Tubular cell proliferation and apoptosis were identified by immunostaining.
Results: After transplantation of WJ-MSC into mice with cisplatin-induced AKI, improvements in renal function and recovery from tubular epithelial cell injury were observed. Several cells engrafted in renal interstitium in the near vicinity of injured tubular epithelia where they exposed their beneficial effects by decreasing tubular cell apoptosis, with no markable effect on tubular cell proliferation.
Conclusions: Infused WJ-MSC can reach damaged kidney tissue after intravenous transplantation. AKI elicited by lethal dose of cisplatin was considerably improved by WJ-MSC, in parallel with less apoptotic events, with no influence on proliferative response.

BO278 THIRD PARTY MESENCHYMAL STROMAL CELL INFUSION IN KIDNEY TRANSPLANT RECIPIENT: 6-MONTH SAFETY INTERIM ANALYSIS

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Background: Mesenchymal stromal cell (MSC) have immunomodulating properties and could be used as immunosuppressive agents. We report the 6-month safety results for the 5 first patients treated with MSC after kidney transplantation (KTx). Here, we address 3 specific safety issues: immunization against MSC and engraftment syndrome defined as acute graft dysfunction not related to rejection and over-immunosuppression.
Patients and method: MSC production was carried out locally. MSC were not matched with kidney recipients' HLA. Included patients were non-immunized, first transplant recipients from deceased donors. MSC (1.5–3.0 × 106/kg) infusion was planned 3 to 5 days post KTx. Patients with cardiovascular instability post KTx were excluded. All patients were treated with Basiliximab induction, Tacrolimus, Mycophenolate Mofetil and Steroid. We prospectively screened for anti-HLA antibodies at month 1, 3 and 6. Informed consent was obtained from all participants. The local ethical committee approved the protocol.
Results: Collectively there were 23/50 and 29/50 HLA mismatches (MM) with kidney and MSC donor respectively, out of which 5 were shared MM. One patient developed de novo DSA, 2 patients anti-HLA antibodies against shared kidney/MSC MM and 1 patient developed 2 specific antibodies against MSC (MSCSA) at month 6. All antibodies were anti HLA class I except for 1. We did not observe any "engraftment" syndrome. Three patients experienced non-severe opportunistic infections: 1 CMV reactivation and 2 polyoma-BK virus viremia.

Recipient	Age at Tx (years)	63 ± 6
	Gender (M/F)	4/1
	BMI (kg/m^2)	27 ± 3
	Dialysis vintage (days)	373 ± 564
Kidney donor	Age (years)	51 ± 18
	Gender (M/F)	3/2
	BMI (kg/m^2)	26 ± 5
	DBD/DCD	4/1
Transplantation	CIT (min)	737 ± 219
	WIT (min)	46 ± 16
	HLA mismatches (*n*)	
	A (0/1/2)	0/4/1
	B (0/1/2)	1/4/0
	Cw (0/1/2)	1/3/1
	DR (0/1/2)	1/4/0
	DQ (0/1/2)	1/4/0
MSC donor	HLA mismatches (*n*)	
	A (0/1/2)	1/2/2
	B (0/1/2)	1/3/1
	Cw (0/1/2)	0/4/1
	DR (0/1/2)	1/3/1
	DQ (0/1/2)	0/3/2

Conclusion: We did not observe any strong safety signal. We did however observe some degree of immunization in 3 patients: 2 developed antibodies against shared kidney/MSC donor HLA MM and 1 MSCSA.

BO279 MESENCHYMAL STEM CELL TREATMENT IN A MOUSE MODEL OF COMBINED LIVER ISCHEMIA REPERFUSION INJURY AND REGENERATION

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Liver ischemia reperfusion injury (IRI) is inevitable during transplantation and extended resections. Hepatic IRI is characterized by hepatocellular injury and hepatocyte loss and may compromise regeneration. At present there is no therapy to treat IRI. Therefore, potential therapeutic strategies to reduce hepatic IRI and accelerate liver regeneration could offer major benefits in both liver transplantation and resection. Mesenchymal stem cells (MSC) are reported to have anti-inflammatory and regeneration promoting properties in models of isolated ischemia or resection. Whether they are of benefit in a more clinically relevant model where IRI is combined with resection induced need for rapid regeneration is currently unknown. Therefore we investigated the effect of MSC administration in a mouse model of combined IRI and partial resection. IRI was induced by occlusion of the blood flow to the left lateral and median liver lobes for 60 min followed by partial hepatectomy of 40% of the liver volume (PH) in C57Bl/6 mice. Animals were treated intravenously with 2-, or 3 x105 mouse syngeneic MSC or PBS control, 2 h before-, or 1 h after IRI. Six hours, and 2- and 5 days after combined ischemia and resection mice were sacrificed. Liver damage was evaluated by measuring liver enzymes, histological damage, and inflammatory markers IL-6 and TNF-α. Liver regeneration was determined by measuring liver/body weight ratio and numbers of proliferating hepatocytes at 2 and 5 days after combined IRI and PH. Liver damage in mice treated with 3 x105 MSC was increased compared to controls. 2 × 105 MSC 2 h before or 1 h after IRI and PH was not significantly different from PBS treated control mice. Liver regeneration was also not different from control animals. In contrast to what is generally assumed, intravenous administration of high numbers of MSC increase liver damage, whereas lower numbers have no beneficial effect on liver IRI or regeneration.

BO280 MULTIPOTENT ADULT PROGENITOR STEM CELL ADMINISTRATION IN A PORCINE MODEL OF EX VIVO LUNG PERFUSION

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Background: Ex vivo lung perfusion (EVLP) is a promising technique to resuscitate potential donor lungs prior to transplantation. Clinical grade multipotent adult progenitor cells (MAPCs) are a novel type of stem cells with immunomodulatory properties. We report our first experience administrating MAPCs during prolonged EVLP comparing intravascular (IV) and intratracheal (IT) administration to modulate ischemia-reperfusion injury.
Materials and Methods: Porcine lungs were perfused for maximum 6 hrs on EVLP following a warm ischemic interval of 90 min. Animals (n = 2/group) were divided in 4 groups. In MAPC-IV group $10*10^6$ MAPCs were administrated IV at onset of EVLP; in CONTR-IV group no cells were added to the perfusate. In MAPC-IT group $10*10^6$ MAPCs in 40 ml PBS were instilled in the airways at onset of EVLP; in CONTR-IT group no cells were added to the PBS. Functional evaluation included the % difference in PVR and Compliance between end and onset of EVLP. Wet-to-dry weight (W/D) ratio was calculated.
Results: Data are depicted as mean.

Not all grafts could be perfused for 6 hrs due to massive edema. Therefore, maximal perfusion time was documented. Decline in graft function was defined as ↑PVR (+%PVR) or ↓compliance (-%COMPL). MAPCs IV further deteriorated lung function and compromised perfusion time compared to CONTR-IV. In contrast, it seems that lung function was better preserved in MAPC-IT compared to CONTR-IT.
Conclusion: These preliminary data indicate that IT administration of MAPCs during EVLP might offer a potential to resuscitate lung grafts. IV administration of MAPCs led to deterioration of pulmonary function in this model. We hypothesize that MAPCs IT might improve epithelial barrier function and modulate the inflammatory response. More data are necessary to confirm these findings and to elucidate potential mechanisms. Results will be updated at time of presentation to n = 6/group.