

BO S052 Next-generation Porcine Low Immunogenicity Anti-Lymphocyte immunoglobulins efficiently delay skin graft rejection in non-human primate

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Induction therapy, with rabbit or horse anti-lymphocyte globulins (ALG) has become a commonplace in transplantation to prevent acute rejection. However, presence of xenogeneic carbohydrates on these immunoglobulins causes short- and long-term adverse effects in human presenting natural antibodies against these epitopes. Infusions of ALG in humans results in formation of immune complexes, allergic reactions, liver toxicity and serum sickness disease when administrated without any other immunosuppressive drugs. To address these issues, we developed LIS1, a new generation ALG from a1,3GT and CMAH knockout swine immunized with a human T cell line. LIS1 efficiently lysed T lymphocytes and, in contrast to other ALG, spared platelets and neutrophils. The aim of this study was to assess the immunosuppressive abilities of LIS1 in a skin allograft non-human primate model.

Five female Cynomolgus monkeys received two skin grafts from an unrelated congener and an autograft as control on the back skin. LIS1 was administrated intravenously over 5 days, starting the day of the graft. Graft were observed every day to establish a grading of graft rejection based on skin necrosis and flexibility. Blood sampling were collected at different time point and histological rejection was assessed on skin biopsies.

Treated animals (n=3) showed a sharp decrease in circulating T lymphocytes between day 1 and 7, recovering by Day 15, in the absence of cytokine release or thrombocytopenia. Histological analysis on day 3 showed that the necrosis caused by tissue ischemia was reduced in treated animals. Skin graft rejection was delayed to Days 19-29 (vs. Day 11 in controls).

In conclusion, LIS1 showed efficacy to delay skin graft rejection. Use of LIS1 might benefit kidney graft recipients by reducing adverse effects of current ALG associated with anti-xenogeneic carbohydrate reactivity.