LS18-031 - Combination cell therapy for immunomodulation in kidney transplantation

Abstract

Outcome after kidney transplantation is unsatisfactory since mandatory immunosuppressive drug therapy is associated with high morbidity and cannot prevent late graft loss. The induction of donor-specific immunological tolerance would be a solution to this clinical problem. However, no tolerance protocol is available for routine clinical use, mainly due to unresolved safety issues. In extensive pre-clinical research, we developed a novel tolerance protocol that combines two types of cell therapy. Treatment with polyclonal recipient T regulatory cells (Tregs) together with the transplantation of donor bone marrow (BM) established tolerance without the need for myelosuppression by irradiation or cytotoxic drugs, thereby substantially improving safety. We therefore propose to perform an academic phase I/IIa, feasibility, safety and efficacy clinical trial in which HLA-mismatched living-donor kidney transplant recipients will be treated with recipient Tregs and donor BM cells without myelosuppressive recipient conditioning. The aim is to demonstrate for the first time that this combination cell therapy is feasible, safe and efficacious and allows the step-wise reduction of immunosuppression so that patients can be maintained on drug monotherapy and might ultimately be completely taken off immunosuppression. The results of this trial are expected to provide proof-of-concept that combination cell therapy is a novel treatment option for immunomodulation in organ transplantation.

Scientific disciplines:
Immunotherapy (70%) | Transplantation medicine (30%)

Keywords:
kidney transplantation, immunology, cell therapy, tolerance, chimerism

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Further links to the persons involved and to the project can be found under
https://wwtf.at/funding/programmes/ls/LS18-031/