New cell therapy approaches yield fewer complications after organ transplantation

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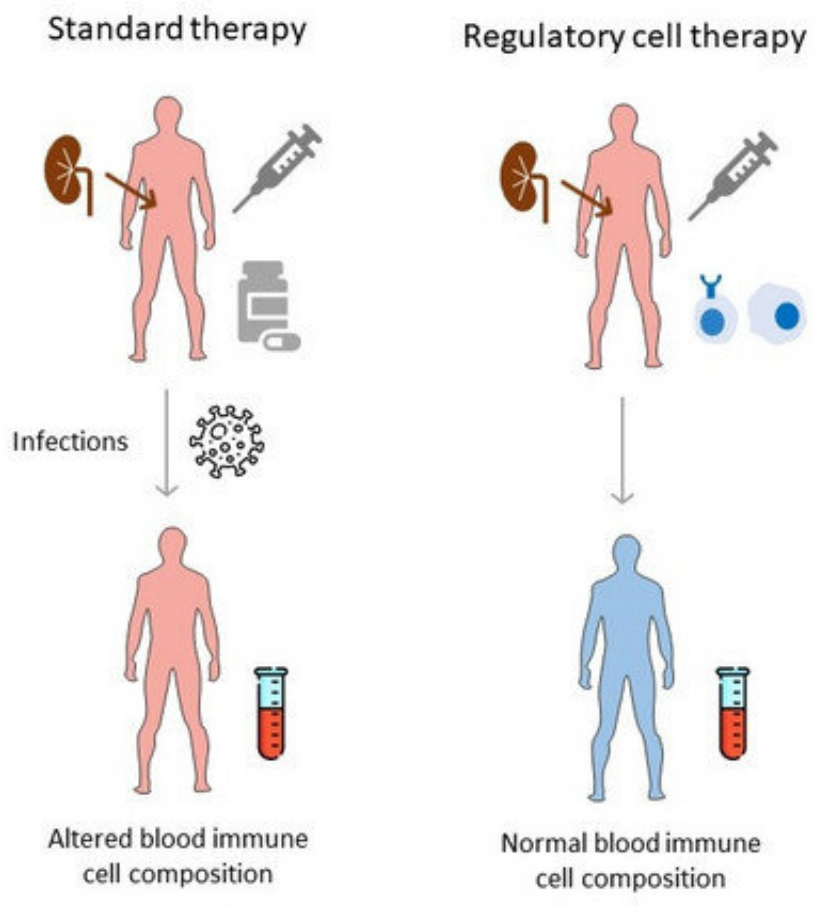

Regulatory cells normalize the immune cells in the blood and prevent serious adverse effects – in contrast to standard therapy with immune depressants. Credit: Sawitzki/ Charité

A large international study coordinated by University Hospital Regensburg and Charité - Universitätsmedizin Berlin has demonstrated the safety of new cell therapy approaches for use in kidney transplant recipients. Transplant recipients were shown to require lower levels of immunosuppression in order to prevent organ rejection. This reduces the risk of side effects such as viral infections. Results from this study have been published in *The Lancet.*

Transplant recipients usually receive immunosuppressants to prevent organ rejection. However, these drugs cannot provide an absolute guarantee that rejection will not occur at a later stage. Furthermore, immunosuppression is often associated with severe side effects such as intolerances, infections or other problems. Cell therapy offers an alternative treatment approach. This involves the use of specific immune cells, which are isolated and expanded in vitro. Known as regulatory cell products, these cells are then infused into the transplant recipient in order to restore their immune system.

Charité was one of a number of institutions involved in the international ONE Study consortium, which was led by Prof. Dr. Edward K. Geissler of University Hospital Regensburg. The Berlin-based members of the consortium were primarily responsible for testing the safety and efficacy of cell therapy in kidney transplant recipients, as well as effects on their immune system. Research centers based in several different countries worked to a standardized protocol to develop a range of regulatory cell products, which were then tested in clinical trials. These therapies, which were administered to transplant recipients either before or after their surgery, comprised regulatory T cell and macrophage products, as well as products made of dendritic cells, which produce anti-inflammatory messengers. Results were then combined and compared with a reference patient group who had received standard-of-care immunosuppression. Patients were then followed up for a further 60 weeks.

"The new cell therapy was able to reduce the need for immunosuppression in approximately 40 percent of patients, thereby minimizing the risk of side effects," says the study's first author, Prof. Dr. Birgit Sawitzki of the Institute for Medical Immunology on Campus Virchow-Klinikum. The regulatory cells were shown to be just as safe as the drugs used in standard treatment and did not result in higher rejection rates. "Particularly remarkable was the fact that none of the patients given regulatory cells developed herpes infections, which often lead to dangerous complications in transplant recipients," notes Prof. Sawitzki.

Prof. Sawitzki's team was primarily responsible for the development and implementation of standardized immune monitoring, i.e., the monitoring of immune cell populations in the blood. "Before transplantation, patients showed altered immune cell composition, and regulatory cells were better than standard therapy at restoring normal composition," explains Prof. Sawitzki. She adds: "This means there are new, safe treatment options which can help to reduce the dose of conventional immunosuppressants and the risk of viral infections." There are plans for further, larger studies to confirm the efficacy of regulatory cell therapy.

More information: Birgit Sawitzki et al, Regulatory cell therapy in kidney transplantation (The ONE Study): a harmonised design and analysis of seven non-randomised, single-arm, phase 1/2A trials, *The Lancet* (2020). DOI: 10.1016/S0140-6736(20)30167-7

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