Asian Transplantation Week 2023

Nov. 15(Wed)~18(Sat), 2023
Conrad Seoul, Korea

Submission No.: CS13-9092
Session : Concurrent Symposium 13 (Kidney/Pancreas)
Date & Time, Place : November 18 (Sat), 15:30-17:00, Room 5F-1
Session Title : New treatment for antibody-mediated rejection

IL-6 inhibitor

Ho Sik Shin
Kosin University Gospel Hospital, Republic of Korea

Chronic antibody-mediated rejection (cAMR) is a significant complication that can occur after kidney transplantation. It is characterized by the presence of donor-specific antibodies (DSA) targeting the transplanted kidney, leading to ongoing inflammation, vascular injury, and ultimately, graft dysfunction. Interleukin-6 (IL-6) is a pro-inflammatory cytokine that plays a role in immune responses, and it has been implicated in various immune-mediated diseases, including transplant rejection. IL-6 inhibitors, also known as IL-6 receptor antagonists, are a class of medications that block the effects of IL-6. Clazakizumab (also known as ALD518) is a humanized monoclonal antibody that targets interleukin-6 (IL-6). Clazakizumab, by inhibiting IL-6, aims to modulate the immune system and reduce inflammation, which can be beneficial in certain immune-mediated conditions, including cAMR after kidney transplantation. These inhibitors have been studied in the context of kidney transplantation, particularly in the management of cAMR, due to their potential to modulate the immune response and reduce inflammation. Research and clinical trials have explored the use of IL-6 inhibitors in kidney transplantation for various purposes, including treating acute rejection episodes and addressing cAMR. Here are some potential ways in which IL-6 inhibitors may be used in the context of cAMR:

1. **Reduction of Inflammation:** IL-6 inhibitors can help reduce the inflammatory response that contributes to graft injury in cAMR. By blocking IL-6 signaling, these drugs may help alleviate some of the damage caused by ongoing immune activity.
2. **Modulation of B Cells:** IL-6 inhibitors can affect the differentiation and function of B cells, which play a role in antibody production. By targeting B cell function, these inhibitors may help reduce the production of donor-specific antibodies that contribute to cAMR.
3. **Adjunct to Standard Therapies:** IL-6 inhibitors may be used as part of a multi-pronged approach to treating cAMR. They may be combined with other immunosuppressive medications, such as corticosteroids, rituximab (which targets B cells), and plasmapheresis to address the immune response and reduce antibody levels.

Unlike current approaches that are broadly targeting B cell proliferation/depletion, or focused on antibody removal/effector blockade, the IMAGINE trial through targeting the IL-6/IL-6R pathway is focused on modulating B cells, plasma cells, regulatory T cells, and potentially effector T cells. Moreover, as chronic active AMR is frequently part of a mixed rejection phenotype, targeting the IL-6/IL-6R pathway may prove particularly effective in this context. Unique to the IMAGINE trial, under the IND, renal function 1-year post-randomization has been accepted by the FDA as a reasonably likely surrogate endpoint. It is critical for the transplant community to finish the IMAGINE study to determine safety and efficacy in a large and rigorous randomized controlled trial.