CAR T Cell Therapy for Autoimmune Diseases: Dawn of a New Era Toward a Cure

By Jeffrey A. Sparks and Matthew A. Sparks

Systemic autoimmune diseases, such as systemic lupus erythematosus (SLE), traditionally require long-term immunosuppression to maintain disease control (1). Although treatment options have expanded over the past few decades, a cure remains elusive (1, 2). A recent case series of outcomes after patients received chimeric antigen receptor (CAR) T cell therapy, published in The New England Journal of Medicine (3), may usher in a new era toward a cure for systemic autoimmune diseases.

CAR T cell therapies are currently approved by the US Food and Drug Administration to treat some types of lymphoma, leukemia, and multiple myeloma (4). These CAR T cell therapies target one of two antigens on B cells: the CD19 or B cell maturation antigen (4), resulting in the death of that specific cell harboring the antigen by the CAR T cell. However, CAR T cell technology could be used to target any antigen, opening up a new platform for targeted therapy.

In the case series (3), investigators in Germany prospectively enrolled 15 patients with refractory systemic autoimmune rheumatic diseases (including SLE, idiopathic inflammatory myositis, and systemic sclerosis) to receive CD19 CAR T cell therapy. CD19 is a transmembrane protein uniquely expressed in both normal and neoplastic B cells, making it an attractive target for immunotherapy. It is expressed on B cell lineages, including plasma cells. The investigators found marked improvements in serologic and clinical markers of disease activity during a median follow-up of 15 months. Most impressively, after the single infusion of CAR T cells, all 15 patients were able to completely discontinue their systemic immunosuppressive medications, an outcome rarely achieved through usual clinical care.

Relevant to nephrologists, among the 8 patients with SLE, all had lupus nephritis, and all resolved proteinuria, normalized complement levels, and had undetectable double-stranded DNA autoantibodies by month 12 (3). Thus, many pharmaceutical companies and rheumatology centers are developing CAR T cell therapy research programs. CAR T cell and other cellular therapies are also being pursued to treat rheumatoid arthritis, inflammatory bowel disease, type 1 diabetes, and multiple sclerosis to prevent organ rejection and treat BK polyomavirus infection, including for kidney transplant recipients (5, 6).

Although these initial results are impressive, some caveats and logistical considerations are needed. The open-label case series was small, uncontrolled, included several heterogeneous diseases, and had a relatively short follow-up. Whereas drug-free remission is thought to be rare, it is not often attempted. B cell depletion with monoclonal antibodies targeting CD20 has been previously studied for lupus nephritis in placebo-controlled studies (7–9), with some infections occurring, including COVID-19, pneumonia, and cellulitis (3). There have been some cases of lymphoma occurring secondary to CAR T cell therapy in patients with cancer (10). Thus, larger controlled studies with a longer follow-up are needed to establish efficacy, safety, and tolerability.

CAR T cell therapy offers a new dawn toward a cure for patients with systemic autoimmune diseases. Other CAR therapies are being investigated that target different antigens and use T regulatory cells that should have less toxicity and do not require conditioning chemotherapy. Nephrologists will be at the forefront of this innovative therapy across myriad indications that will include lupus nephritis, systemic vasculitis, kidney transplant, and glucocerebrosidosis.

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References

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