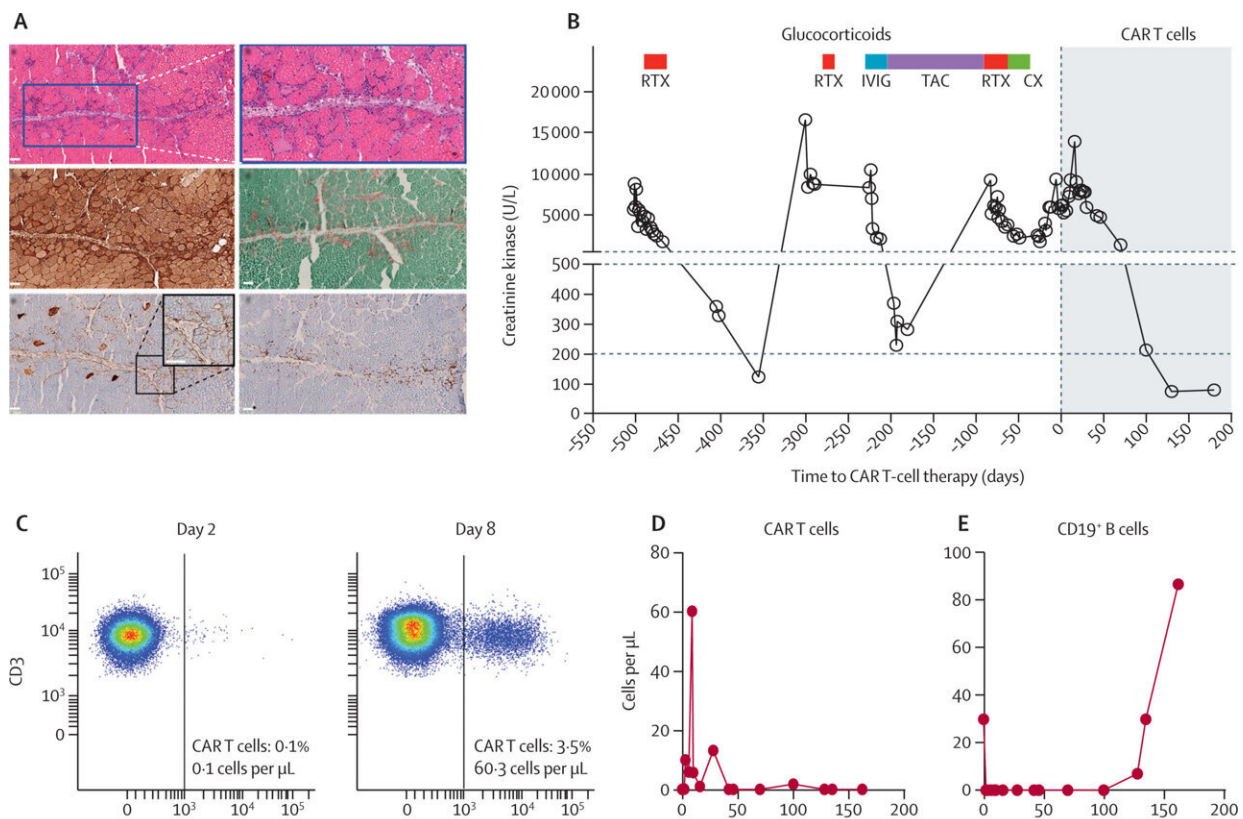


Testing their strength: CAR T-cells combat muscle inflammation

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Effects of CAR T cells on the manifestations of antisynthetase syndrome. (A) Neuropathology. Top, haematoxylin and eosin staining showing predominant perifascicular muscle atrophy and necrotic muscle fibers. Center left, staining for MHC-1 showing ubiquitous expression on muscle fibers with predominance at the perifascicular borders. Center right, connective tissue or perimysial fragmentation depicted by acid phosphatase staining. Bottom left, C5b9 staining showing sarcolemmal decoration of muscle fibers with predominance at the perifascicular borders and few sarcoplasmatic stained fibers. Bottom right, CD3

staining showing T-cell infiltrates invading the endomysial compartments and originating from the perimysial region. Scale bars=100 μ m. (B) Creatinine kinase concentrations before and after treatment with CD19 CAR T cells and the timing of previous treatments. The horizontal line indicates the upper limit of normal range. (C) Dot plots showing the expression of CD3 and CD19 CAR in circulating CD19 CAR T cells, quantified by FACS on day 2 and day 8 after infusion. (D) Concentration of circulating CD19 CAR T cells over time. (E) Concentration of CD19+ B cells over time. (F) Disease activity assessed using the PGA (left), PtGA (middle), and MMT8 (right) measures. (G) Concentrations of serum creatinine kinase (left) and autoantibodies against Jo-1 (right) over time. Dashed lines show the upper limit of normal range. (H) Disease activity assessed with the EMDA scale. (I) Disease activity assessed with the ACR/EULAR TIS, showing cutoffs for major, moderate, minor, or no improvement. (J) MRI. Top left, baseline coronal axial T2-weighted, fat-suppressed sequence shows the longitudinal extent of the hamstring pathology on both sides (asterisks). Bottom left, the corresponding axial MRI shows diffuse oedematous changes reflecting myositis of almost all thigh muscle groups, but primarily of the quadriceps muscles (asterisk). Marked fasciitis is also seen, particularly in the vastus medialis and semitendinosus muscles (arrows). Top right, complete resolution of muscle and fascial inflammatory alterations 3 months after treatment. Bottom right, corresponding axial MRI confirms that healthy muscle signal has been restored in the quadriceps and the hamstrings. (K) Chest CT scans. Left, baseline coronal reformatted CT scans showing bilateral basal opacities (arrows) and right upper lobe opacities consistent with alveolitis. A reticular abnormality reflecting interstitial lung disease can also be seen. Right, CT scans obtained 3 months after initiation of therapy show complete resolution of right upper lobe findings (asterisk) and alveolitis, and minor residual findings of basal interstitial lung disease (arrows). RTX=rituximab. IVIG=intravenous immunoglobulins. TAC=tacrolimus. CX=cyclophosphamide. CAR=chimeric antigen receptor. FACS=fluorescence-activated cell sorting. VAS=visual analog scale. PGA=physician global assessment. PtGA=patient global assessment. MMT8>manual muscle testing score 8. EMDA=extramuscular disease activity. ACR/EULAR TIS=American College of Rheumatology/European League Against Rheumatism total improvement score. Credit: *The Lancet* (2023). DOI: 10.1016/S0140-6736(23)00023-5

Universitätsklinikum Erlangen is the first in the world to use CAR T-cells to successfully treat a patient suffering from a severe case of muscle inflammation (myositis). The disease is triggered by a malfunction in the immune system that leads to inflammation of the muscles, and the risk of developing a very severe form of the disease is high. *The Lancet* has now published news of the successful treatment in a case report.

When the 41 year old Mr. S. noticed a dramatic deterioration in his health last year, he initially put it down to a viral infection. However, his health took a dramatic turn for the worse when he was suddenly no longer to move more than a few feet and was barely able to stand up. His symptoms were caused by a severe autoimmune disease affecting his muscles, joints, skin and lungs belonging to the group of anti-immune muscle [inflammatory diseases](#) (myositis). The diagnosis: anti-synthetase syndrome.

The name anti-synthetase syndrome is derived from the observation that the enzymes required for the synthesis of amino acids known as aminoacyl-tRNA synthetases are attacked in error by the immune system. This severely impacts the function of various cells.

Modifying patients' own immune cells gives hope for the future

"Autoimmune inflammatory muscle diseases are severe diseases that can end fatally if they are diagnosed at too late a stage or patients fail to react sufficiently to medicines aimed at suppressing the immune system," explains Prof. Dr. Georg Schett, Director of the Department of Medicine 3—Rheumatology and Immunology at Universitätsklinikum Erlangen.

In the case of Mr. S., all traditional treatments used to suppress the [immune system](#) failed. He was saved by CAR T-cells: "CAR T-cells are immune cells withdrawn from the patient's blood and genetically engineered to carry a [chimeric antigen receptor](#) (CAR)," explains Prof. Andreas Mackensen, Director of Department of Medicine 5—Hematology and Oncology. "Once the cells are returned to the patient's body, the CAR allows the modified [immune cells](#) to specifically target the cells triggering the disease."

Complete recovery after six months

After receiving the infusion of CAR T-cells, Mr. S. experienced a dramatic improvement in his health: the inflammation in his muscles, lungs and joints relapsed almost entirely. His strength, performance and stamina returned. "What was particularly surprising was that Mr. S. was able to stop taking all immune-suppressive medicine and in particular corticosteroids without the disease flaring up again," said Dr. Fabian Müller (Department of Medicine 5), who is caring for the patient. Six months after receiving the CAR T-cells, Mr. S. has recovered entirely from his autoimmune disease.

"It acted like pressing a reset button! Before treatment I could do nothing, and now I'm functioning like normal again," says Mr. S. This is the second type of autoimmune disease that physicians and researchers at the Deutsches Zentrum Immuntherapie (DZI) at Universitätsklinikum Erlangen have successfully treated using CAR T-cells. In the first instance, the cells excelled in treating systemic lupus erythematosus (SLE).

Other patients suffering from myositis or SLE will be offered the opportunity of benefiting from CAR T-cell treatment as part of the clinical CASTLE study, starting this year.

More information: Fabian Müller et al, CD19-targeted CAR T cells in refractory antisynthetase syndrome, *The Lancet* (2023). [DOI: 10.1016/S0140-6736\(23\)00023-5](https://doi.org/10.1016/S0140-6736(23)00023-5)

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