

Case report: Severe systemic lupus no longer detectable after cancer medication treatment

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No more indications of systemic lupus can currently be found after the therapy with the bispecific antibody, either in the laboratory or clinically. Credit: Charité | Arne Sattler

Universitätsmedizin Berlin is astounded by the huge improvement seen



in a female patient with severe systemic lupus erythematosus (SLE) after being treated with the cancer medication teclistamab. Not long ago, the 23-year-old was wheelchair-bound due to the autoimmune disease.

Nearly six months after starting <u>treatment</u>, the patient is now completely symptom-free. Only time will tell if this improvement will last over the long term, but the case—which the team has now <u>published</u> in the *New England Journal of Medicine*—marks a promising starting point for further studies.

Nothing was sufficiently alleviating the symptoms of the 23-year-old patient from Berlin, including cortisone and eight other therapies that should have moderated her overactive immune system.

Her autoimmune disease, diagnosed as <u>systemic lupus erythematosus</u>, was particularly severe and was attacking four of her organ systems. Her skin was blistered, her joints and kidneys were severely inflamed, and her number of red blood cells, which supply oxygen to the body's tissues, was too low.

"Due to the <u>persistent pain</u> she was experiencing, the patient could no longer walk, was wheelchair-bound, and her kidneys were at risk of failing," says Dr. Tobias Alexander, the physician treating her at the Department of Rheumatology and Clinical Immunology at Charité. As the Head of the Rheumatology Outpatient Clinic, he'd "never seen a case this severe before."

Because the established treatment pathways had all been exhausted, he suggested that the patient should take teclistamab—the first time this had been tried. Teclistamab is a bispecific antibody that is approved for the treatment of multiple myeloma, a cancer of <u>plasma cells</u> in the bone marrow.



In systemic lupus erythematosus, plasma cells produce autoantibodies, which are antibodies that target the body's own tissue.

Alexander, a consultant rheumatologist, explains, "Teclistamab is highly effective at destroying the plasma cells and also works against their progenitor cells, which would otherwise quickly produce new plasma cells. We therefore presumed that the cancer medication could eliminate the cause of the systemic lupus and help the patient for the long term."

Disease no longer detectable after five injections

With the patient's consent, the drug was prescribed "off-label." The therapy was delivered on an inpatient basis at the Department of Hematology, Oncology and Cancer Immunology on Charité Campus Benjamin Franklin and proved successful: Five injections of the cancer medication administered under the abdominal skin over a period of five weeks gradually relieved the patient's symptoms.

Within a few weeks, her <u>kidney function</u> and <u>blood levels</u> improved and her skin and joint inflammation completely subsided. Since mid-April, no more autoantibodies have been detected in the 23-year-old's blood, even though the treatment with immunosuppressants was stopped before the start of the therapy and cortisone was no longer administered after six weeks.

"The patient is in full remission," says Alexander.

"That means she's no longer experiencing any symptoms of her disease and we can no longer find any indication of systemic lupus, either clinically or in the laboratory. It would be too early to say that she's cured, but such powerful results are an absolute exception in rheumatology and are all the more remarkable considering that none of the available treatment approaches had been sufficiently effective



beforehand.

"Above all, the success of the therapy, of course, signifies an immeasurable improvement in the patient's quality of life, which we're delighted about. However, we don't know yet how long the positive effects will last. Because the results are provisional, the therapy is not yet suitable for wider use."

Risks of the treatment

The drug's major intervention in the immune system also presents some considerable risks. For example, immune cells may produce excessive amounts of inflammatory mediators. Depending on its progression, this kind of cytokine release syndrome can be life-threatening. The patient treated at Charité also developed severe cytokine release syndrome during the teclistamab therapy, developed pneumonia and sinusitis, and the number of protective antibodies in her blood fell.

"These side effects are much more serious than those experienced in conventional rheumatological therapies and sometimes required inpatient treatment," says Prof. Jan Krönke, who oversaw the patient's oncological treatment. "But they are consistent with the reactions that teclistamab triggers in patients with multiple myeloma, so they were not unexpected."

To determine how long the positive effects of teclistamab last, the treatment team is still closely monitoring the patient and her immune system's activity. If they prove to be long-term and are confirmed in further studies, Alexander believes the cancer medication's potential benefits in rheumatology could be huge.

"For now at least, teclistamab's therapeutic results for the patient are comparable with the impact of CAR T-cell therapies. The difference



being that the bispecific antibody is much easier to use and can be administered over a shorter period, which would be an enormous advantage."

CAR T-cell therapies are new treatment methods that have been able to keep autoimmune diseases at bay for years in individual cases. However, they require chemotherapy and gene therapy and are very timeconsuming and resource-intensive.

More information: Tobias Alexander et al, Teclistamab-Induced Remission in Refractory Systemic Lupus Erythematosus, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMc2407150

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