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## Rethinking SLE Treatment: Recent Approvals, Novel Targets, and What's Next

### Dr. Jackson:

This is *Living Rheum* on ReachMD. I'm Dr. Steve Jackson, and today, I'm joined by Dr. Marc Scherlinger, who will be updating us on the latest treatment advances in systemic lupus erythematosus, or SLE. Dr. Scherlinger is a Clinical Chief at the Strasbourg University Hospital in France, and he co-authored an article on this topic that was published in *Nature* in July 2025.

Dr. Scherlinger, welcome to the program.

### Dr. Scherlinger:

Hi, Steve. Thank you for having me, and please call me Marc.

### Dr. Jackson:

Absolutely. So, Marc, let's get started with the big picture. How has our approach to SLE treatment transformed over the last few decades, and where does the focus now lie?

### Dr. Scherlinger:

Thank you for this great question, Steve. It's indeed a very important point. In the last decades, there has been a real paradigm change in the treatment of lupus. At the time, our main aim was to treat the patient as though there was less inflammation, and the patient was feeling better.

But now, we have shifted into a real treat-to-target approach. Our aim is to have very low disease activity or no disease activity without corticosteroid treatment because we know that these corticosteroids—even a very low dose—in the long term are going to make organ damage occur in the patient. So basically, this is the change in the approach to treatment. And for the last 60 years, we've been using corticosteroids, of course, and mainly nonspecific immunosuppressive drugs that have been developed for other diseases. I think SLE is one of the most exciting autoimmune diseases right now because there are so many drugs in development in it.

Of course, this development has come with a better understanding of systemic lupus pathogenesis with the importance of, for example, B cells, but also specific cytokines, such as type I interferon. And of course, with a better understanding of the disease, there's also a better understanding of the individual patients because systemic lupus is a very heterogeneous disease, and not a patient is the same as another. And even in one patient, the disease can evolve with time. At the beginning, it can be highly dependent on interferon and then shift toward other physiopathological mechanisms, and so we are driving toward more precision medicine and a more targeted approach to treatment.

### Dr. Jackson:

Thank you. So in your article, you do describe this shift away from broader immunosuppression. Can you tell us now about some targeted therapies currently showing promise?

### Dr. Scherlinger:

We have had, in the last few years, two monoclonal antibodies that have been approved in SLE. It was quite new because since corticosteroids have not been an approved drug specifically in SLE, so it was a great leap forward. So these are belimumab, which targets B cell cytokine, and anifrolumab, which targets type I interferon. They are already being used and have shown quite nice effect in terms of improvement of remission attainment. But even with this drug that indeed improved the treatment of patients, we are still far from the 100 percent of patients with remission without corticosteroid, and therefore, there is still a need to improve the care and develop new drugs.

There are more than 100 drugs currently in development in systemic lupus, so it's quite a complex field. One exciting thing is, of course, intracellular signaling, because we know that blocking one cytokine, you know that there is always another cytokine that will come up, so going deeper in the cell signaling will allow to block a cytokine at the same time. And we can think of blocking JAK with JAK inhibitor, but also a BTK, which is a kinase involving B cell signaling. So these are quite interesting strategies that are being developed.

**Dr. Jackson:**

Now, one especially intriguing idea is the potential use of CAR T cells. How is this approach being adapted for SLE?

**Dr. Scherlinger:**

Yeah. So CAR T cells are a very exciting therapy that is being investigated in systemic lupus. As you know, they have been developed in onco-hematology to treat blood cancer and among them to destroy B cells. And of course, in lupus, we want to eliminate autoreactive B cells, so it makes sense to use them.

And T cell has been tried first in Germany by Georg Schett in Erlangen with very nice results in patient by targeting CD19 B cells, so mostly quite widely the B cell. And early clinical data that come, of course, from open studies are really exciting because for maybe the first time with patients with highly refractory disease, we can reach an off-treatment, long-term remission that may even ask the question of a long-term remission or even a cure in these patients. So we don't want to go ahead and talk about curing lupus because it's quite early in the field, but these therapies have definitely generated a lot of hope among physicians and patients.

**Dr. Jackson:**

And there's strategies like regulatory T cell therapies and low-dose interleukin-2. How do they fit into this evolving treatment landscape?

**Dr. Scherlinger:**

Yeah, that's a great question because lupus is characterized by loss of tolerance, and ideally, we want to restore this tolerance. The issue is that Treg treatment and low-dose IL-2 to stimulate the Treg cell—there's been a lot of studies on them, and the results have been quite heterogeneous. Several studies which are uncontrolled have shown excellent results, but the most randomized clinical trial studies were not that exciting. And I think it's because of the way we use it. Probably, we might need to use a suppressive drug to induce the remission and then use this kind of therapy to keep the patient under long-term remission. And it might be that using low-dose IL-2 or Treg cell in patients with high disease activity and with a lot of inflammation is not efficient enough, which may explain the lack of efficacy in the future.

**Dr. Jackson:**

Okay, thank you for that. For those just tuning in, you're listening to *Living Rheum* on ReachMD. I'm Dr. Steve Jackson, and I'm speaking with Dr. Marc Scherlinger about the treatment advances in systemic lupus erythematosus.

Marc, if we look ahead, how realistic is the idea of durable remission for patients with SLE based on these emerging treatment approaches?

**Dr. Scherlinger:**

I think we want to be optimistic and hope that it will be possible for most of our patients, but we have to remain calm and look at the data. I think it's quite possible, and they are accruing data using emerging treatment approaches showing that most patients improve in the long term even if there might remain some symptoms and some autoantibodies. But probably, we may need to combine treatment in these patients because lupus is very heterogeneous, and when you block a pathway, another one will light up.

And so I think it's completely doable, but we need several things. We need new drugs, of course, but we also need a strategy trial. We need to know how to better use the drugs that we have and which order and for which patient.

**Dr. Jackson:**

Absolutely. And finally, what challenges remain in translating these emerging therapies into real-world clinical practice? And how can we address those gaps?

**Dr. Scherlinger:**

Yeah. So these emerging therapies are really exciting, but as you say there are many issues to really adopt them in the current practice. They are costly. They are difficult to set in place. They necessitate long hospitalization for follow-up. So we probably need several things.

First, we need, as rheumatologists, to learn about these treatments and to learn how to use them, and probably, in the near future, these treatments, such as CAR T cell and T cell engager, will go out of the hematology department and will be used directly into rheumatology department, as it was the case with monoclonal antibody and rituximab at the time. Then, we need to have a better strategy for the patient and how to choose the best treatment for the right patients. And this is a very exciting area of research with biomarker

development. And finally, we need to have a better understanding of what these treatments do to our patients in the long term because in the end, it's improving the patients long term and also improving the quality of life, and I think we need it for continued research and evidence.

**Dr. Jackson:**

And that's a great way to round out our discussion. I want to thank my guest, Dr. Marc Scherlinger, for joining me to discuss new and emerging approaches in systemic lupus erythematosus care. Dr. Scherlinger, it was a pleasure having you on the program.

**Dr. Scherlinger:**

Thanks for having me, and take care.

**Dr. Jackson:**

And for ReachMD, I'm Dr. Steve Jackson. To access this and other episodes in this series, visit *Living Rheum* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.