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LETTER TO THE EDITOR Open Access

Systemic lupus erythematosus therapies: a decade of progress and prospects in clinical trials

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Dear Editor,

Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by chronic inflammation, immune dysregulation, and multi-organ involvement. The disease can affect people of all ages, with a higher prevalence in women of childbearing age. The pathogenesis of SLE involves the interaction of genetic, environmental, and immunologic factors leading to the production of autoantibodies and immune complexes that cause tissue damage [1]. Current therapeutic strategies focus on symptom management and immunosuppression, but these therapies are often accompanied by significant side effects and fail to address the underlying disease mechanisms [2]. Therefore, exploring new therapeutic approaches is essential to improve the prognosis and quality of life of patients with SLE.

We searched the ClinicalTrials.gov (https://clinicaltrials.gov) database using the keyword "systemic lupus erythematosus" for the period January 1, 2014, to December 31, 2024, depending on the study phase. A total of 286 trials were included based on study phase, study status, and intervention.

There is an overall upward trend in research on SLE from 2014 to 2024, peaking in 2024, an increase that reflects the growing interest in SLE research and the continued search for new therapies. However, there was a small decline in 2020, which may be attributed to the impact of the COVID-19 outbreak on research activities and patient recruitment (Fig. 1A). The high proportion of "completed" trials suggests that many studies have reached their endpoints, but the limited number of approved therapies highlights the challenge of translating research results into clinical practice (Fig. 1B). The majority of SLE clinical trials fall into the phase I and II and junction phases (68%), with relatively few phase III and IV trials (24%), a phenomenon that suggests the need for larger studies to confirm the safety and efficacy of new therapies (Fig. 1C).

Immunotherapy is the most popular approach in SLE clinical trials, followed by targeted therapies and stem cell transplantation, among others (Fig. 1D). Current drug research is focused on targeting B cells, T cells, and cytokines. Since the approval of belimumab for active SLE in 2011, it has become the main clinical treatment. However, such as intolerance to belimumab or other significant side effects, there has been an upsurge in research on novel therapeutic agents (including Anifrolumab and Stem Cell Transplantation as well as Cenerimod), none of which are in clinical phase IV, and so there is a need to monitor the performance of the drugs in real-world clinical applications before further evaluating their long-term safety and efficacy (Fig. 1E).

Mesenchymal stem cells (MSC) work through various mechanisms such as immune regulation, tissue repair, cellular autophagy and extracellular vesicles, which

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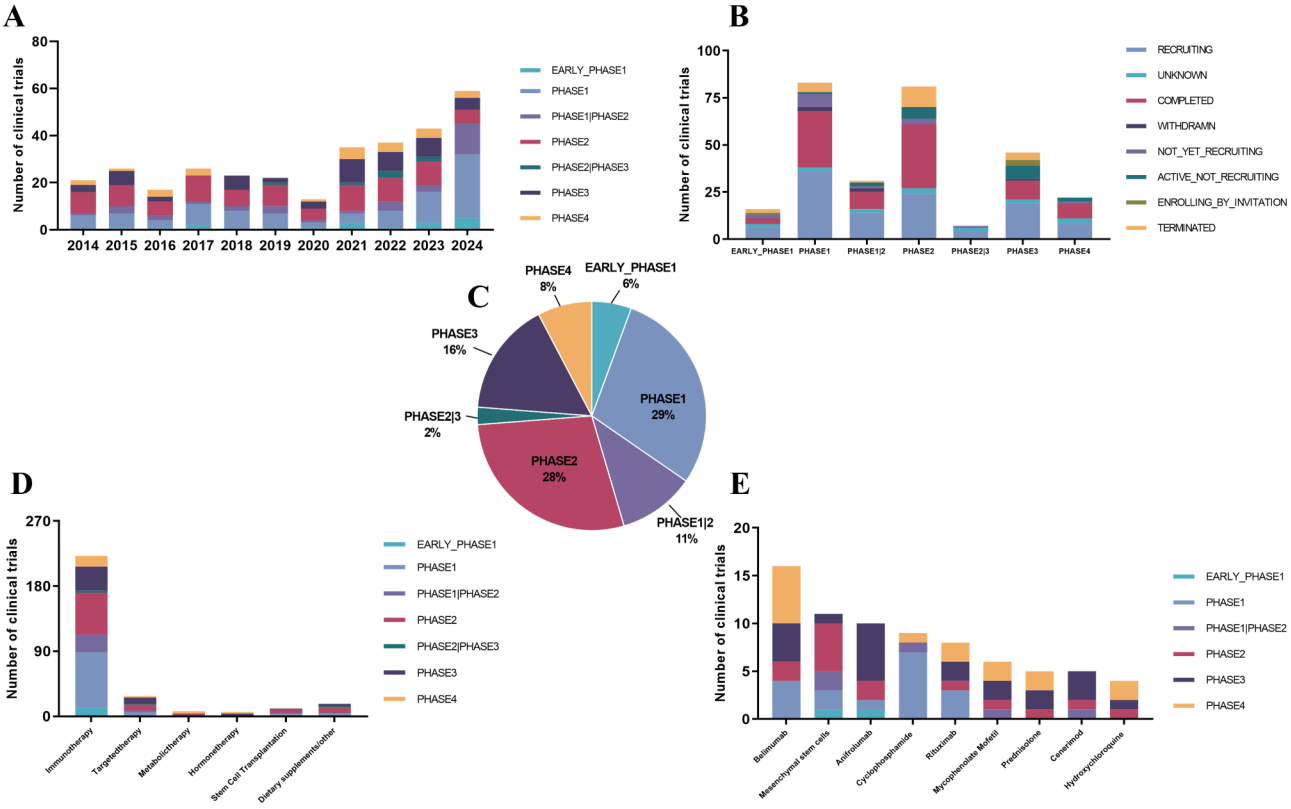

Fig. 1 Global SLE Clinical Trials Landscape. **A**, number of clinical trials in SLE in the last 10 years; **B**, distribution and status of clinical trials in different phases from 2014 to 2024; **C**, Clinical phases of SLE clinical trials; **D**, The clinical stages of the primary treatment modalities; **E**, 9 most commonly used types of therapeutic drugs

can inhibit the over-activation of immune cells, reduce inflammatory responses and promote the repair of damaged tissues, and are currently mainly in the phase I-II clinical trial stage [3]. Clinical studies have shown improvement in renal function and hematological indices in patients after MSC transplantation and no serious adverse events have been reported, suggesting that it has a promising application in the treatment of SLE and shows potential in the treatment of SLE [4, 5].

Despite progress in SLE clinical trials, some limitations remain. First, the heterogeneity of SLE patients is characterized by diverse clinical presentations and genetic backgrounds, which creates challenges in the design and interpretation of clinical trials. Second, long-term safety and efficacy measurements of new therapies, especially in combination regimens, need to be further evaluated in larger and longer trials.

In summary, the state of clinical trials for SLE therapies has evolved significantly over the past decade, with a focus on immunotherapy. However, the limited number of phase III and IV trials and approved therapies highlights the need for continued research efforts. Future studies should aim to address these limitations, explore new therapeutic targets, and optimize therapeutic strategies to improve the prognosis of SLE patients.

Supplementary Information

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Supplementary Material 1

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Author contributions

Wang ZW, Gao SY, Zhu Y were responsible for the literature collection and drafting the paper.; Chen LL supervised the study. All authors read and approved the final version the manuscript.

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Data availability

The data used in this study are available from the ClinicalTrials.gov database (https://clinicaltrials.gov).

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References

1. Gómez-Bañuelos E, Fava A, Andrade F. An update on autoantibodies in systemic lupus erythematosus. Curr Opin Rheumatol. 2023;35(2):61–7.
2. Siegel CH, Sammaritano LR. Systemic lupus erythematosus: a review. JAMA. 2024;331(17):1480–91.
3. Mathias LM, Stohl W. Systemic lupus erythematosus (SLE): emerging therapeutic targets. Expert Opin Ther Targets. 2020;24(12):1283–302.
4. Li A, Guo F, Pan Q, Chen S, Chen J, Liu HF, Pan Q. Mesenchymal stem cell therapy: hope for patients with systemic Lupus Erythematosus. Front Immunol. 2021;12:728190.
5. Shin JC, Kim KN, Yoo J, et al. Clinical trial of human fetal brain-derived neural Stem/Progenitor cell transplantation in patients with traumatic cervical spinal cord Injury. Neural Plast. 2015;2015:630932.

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