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Efficacy and Safety of Anifrolumab in Systemic Lupus Erythematosus (SLE): A Systematic Review of PubMed Literature

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Abstract

Systemic lupus erythematosus is a heterogeneous autoimmune disease characterized by loss of immune tolerance, widespread inflammation, and multiorgan damage. Despite advances in treatment, many patients remain restricted to standard therapies. Type I interferon signaling has been identified as a key factor leading to the development of more targeted therapy, including, Anifrolumab, which is a fully human monoclonal antibody that binds to type I interferon receptor subunit 1 (IFNAR1) and inhibits interferon signaling. To review clinical evidence on efficacy and safety of anifrolumab in adults with SLE, to evaluate whether targeting the type I interferon pathway represents an effective therapeutic approach. PubMed literature search was conducted to identify clinical studies evaluating the efficacy and safety of anifrolumab in adult patients with moderate-to-severe SLE, including randomized controlled trials, long-term extension studies, post-hoc analyses, translational studies, and Japanese sub-analyses. Across the reviewed clinical studies, anifrolumab consistently improved disease activity. Most trials reported higher response rates in anifrolumab-treated participants than in

placebo-treated participants, particularly in global disease activity scores and skin-musculoskeletal manifestations, correlating with suppression of the type I IFN gene signature. Anifrolumab was generally well tolerated, with mostly mild to moderate adverse events. The most frequently reported side effects included upper respiratory tract infections, nasopharyngitis, bronchitis, and herpes zoster, with overall tolerability comparable to placebo. Anifrolumab (300 mg IV every 4 weeks) appears to be a well-tolerated, effective therapeutic option in the management of SLE, with a favourable safety profile and reduced incidence of serious adverse events compared with placebo.

Keywords: Anifrolumab, Systemic Lupus Erythematosus (SLE), Type I interferon, interferon signaling, multiorgan damage, autoimmune disease.

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease driven by multisystem involvement. This multisystem disorder is also multifactorial and can result from a combination of genetic, environmental, immunological, and hormonal factors that activate both innate and adaptive immunity (Ameer et al., 2022). SLE is characterized by the production of autoantibodies, phases of flare-ups and remission (Accapezzato et al., 2023), and persistent inflammation, as the body's immune system mistakenly attacks healthy tissues, causing widespread tissue damage and significantly affecting organs such as the skin, joints, kidneys, heart, lungs, and brain (Shiozawa, 2025). Although the symptoms vary widely among individuals, they include, but are not limited to, fever, mouth or nose ulcers, swollen joints, a distinctive "butterfly" rash on the face, and weight loss (Hoi et al., 2024). SLE can have several phenotypes varying from mild cutaneous and musculoskeletal involvement to multiorgan and

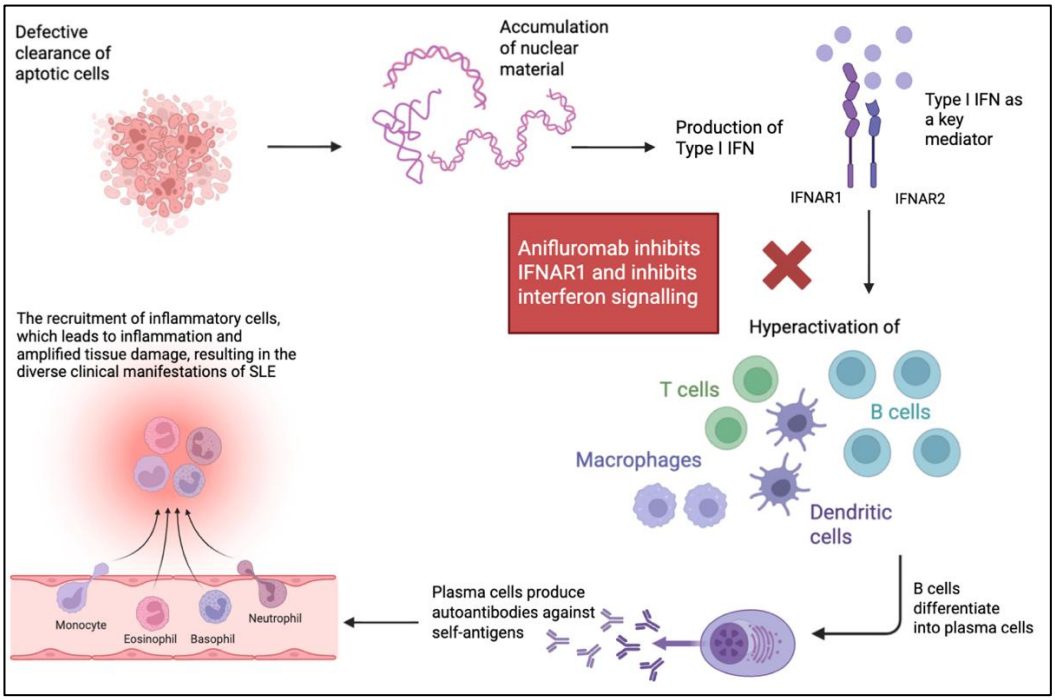
severe central nervous system involvement, leading to potentially life-threatening cardiovascular complications like lung and heart inflammation, kidney disease, lupus nephritis, arthritis, and neuropsychiatric symptoms such as seizures (Yu et al., 2021).

Several immunopathogenic pathways contribute to the development of SLE, leading to dysregulation of cells of both innate and adaptive immunity (Figure 1). This leads to T-cell activation of autoreactive B cells, resulting in the deposition of immune complexes in tissues and initiating an autoimmune cascade that spreads throughout the body. These factors can further contribute to the loss of immunological tolerance, leading to the formation of pathogenic autoantibodies that cause tissue damage through multiple mechanisms (Arnaud et al., 2024). In healthy individuals, dying cells are efficiently eliminated, preventing the activation of immune cells against self-components. However, in SLE, this clearance of apoptotic cells is altered, leading to the accumulation of nuclear material, such as DNA and RNA, that is mistakenly recognized as foreign by the immune system (Tsokos et al., 2016). Further, type I interferons (IFN) play a significant role in the development of SLE by promoting abnormal immune activation and stimulating dendritic cells, macrophages, B cells, and T cells. This process persuades the expression of several interferon-stimulated genes, which correlate with disease activity and severity (Accapezzato et al., 2023). As these cells become hyperactivated, B cells differentiate into plasma cells and produce autoantibodies against self-antigens, including anti-nuclear antibodies (ANA), anti-double-stranded DNA (anti-dsDNA), and anti-Smith (anti-Sm) antibodies. These autoantibodies are considered as hallmarks of SLE as they are involved in disease progression because they form immune complexes when they bind to circulating self-antigens, triggering the activation of the complement system and the recruitment of

inflammatory cells, such as neutrophils and macrophages, which leads to inflammation and amplified tissue damage, resulting in the diverse clinical manifestations of SLE (Lou et al., 2022). Collectively, these immunological events are primarily driven by the dysregulated type I interferon signaling, underscoring it as a therapeutic target in patients with SLE (Bruera et al., 2023).

Figure 1

Pathophysiological Mechanism of Systemic Lupus Erythematosus (SLE) Development and Action of Anifrolumab in Preventing SLE.



Note. This figure was created in BioRender.com.

Despite the recent advances in technology and understanding of the pathological basis and risk factors for SLE, the exact pathogenesis is still not well known, which is why this disease still poses a significant mortality risk in patients. To manage this condition, current therapies include

several immunosuppressant agents, corticosteroids, and BAFF (B-cell activating factor)/APRIL (a proliferation-inducing ligand) inhibitors, but these approaches are limited by inadequate disease control and potential toxicity (Touma & Gladman, 2017). Anifrolumab is a fully human monoclonal antibody that binds to type I interferon receptor subunit 1 (IFNAR1) and inhibits interferon signaling (Figure 1) (Deeks, 2021). This prevents type I interferons (including IFN-α, IFN-β, and IFN-ω) from binding their receptors, reduces the hyperactivity of immune cells, and lowers the expression of interferon-stimulated genes by disrupting the processes of autoantibody production and inflammation. This mechanism restores the balance between innate and adaptive immune responses. It addresses the need for a more targeted therapeutic approach to SLE than traditional immunosuppressants, highlighting the potential of anifrolumab to reduce disease activity, lower flare frequency, and limit organ damage. This systematic review paper aims to evaluate the efficacy and safety of anifrolumab for the treatment of SLE by analyzing current literature, including randomized controlled trials and related studies from PubMed, and provide a comprehensive understanding of its therapeutic potential and implications for clinical practice.

Methods

Study design and research

We conducted a search examining Anifrolumab therapy for SLE patients. Literature searches were performed in PubMed (between Feb 14, 2013, and August 2, 2025). The retrieval strategy combined the following key words and Medical Subject Headings (MeSH) terms: ((anifrolumab) AND (Systemic Lupus Erythematosus [MeSH Terms])) AND (clinical trial

[Publication Type]). The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Study selection/ inclusion criteria

For this review, studies were selected based on predetermined eligibility criteria to ensure relevance and quality. 1) Studies were required to evaluate the efficacy and/or safety of anifrolumab or other type I interferon pathway inhibitors. 2) Only clinical studies conducted on human participants with systemic lupus erythematosus (SLE) were considered. 3) Articles were included only if they were available in English and provided complete and valid data on clinical outcomes or adverse events. 4) Studies that did not meet these criteria were excluded. 5) Animal experiments, non-comparative or non-randomized designs (*e.g.,* case-control, cross-sectional studies), and studies with incomplete or missing outcome data were excluded from analysis. 6) Non-original research (*e.g.,* systematic reviews, meta-analyses, guidelines, conference abstracts, or editorials) was not included.

Statistical analysis

Data for adverse effects were analyzed using GraphPad Prism (version 10). For each adverse event, the percentage of affected patients in the anifrolumab and placebo groups was obtained from published clinical trials. Each dot represents a single study. Differences between treatment groups were assessed using multiple t-tests with Holm-Sidak correction. Statistical significance was defined as * $P<0.05$, ** $P<0.01$, and ns (not significant).

Results

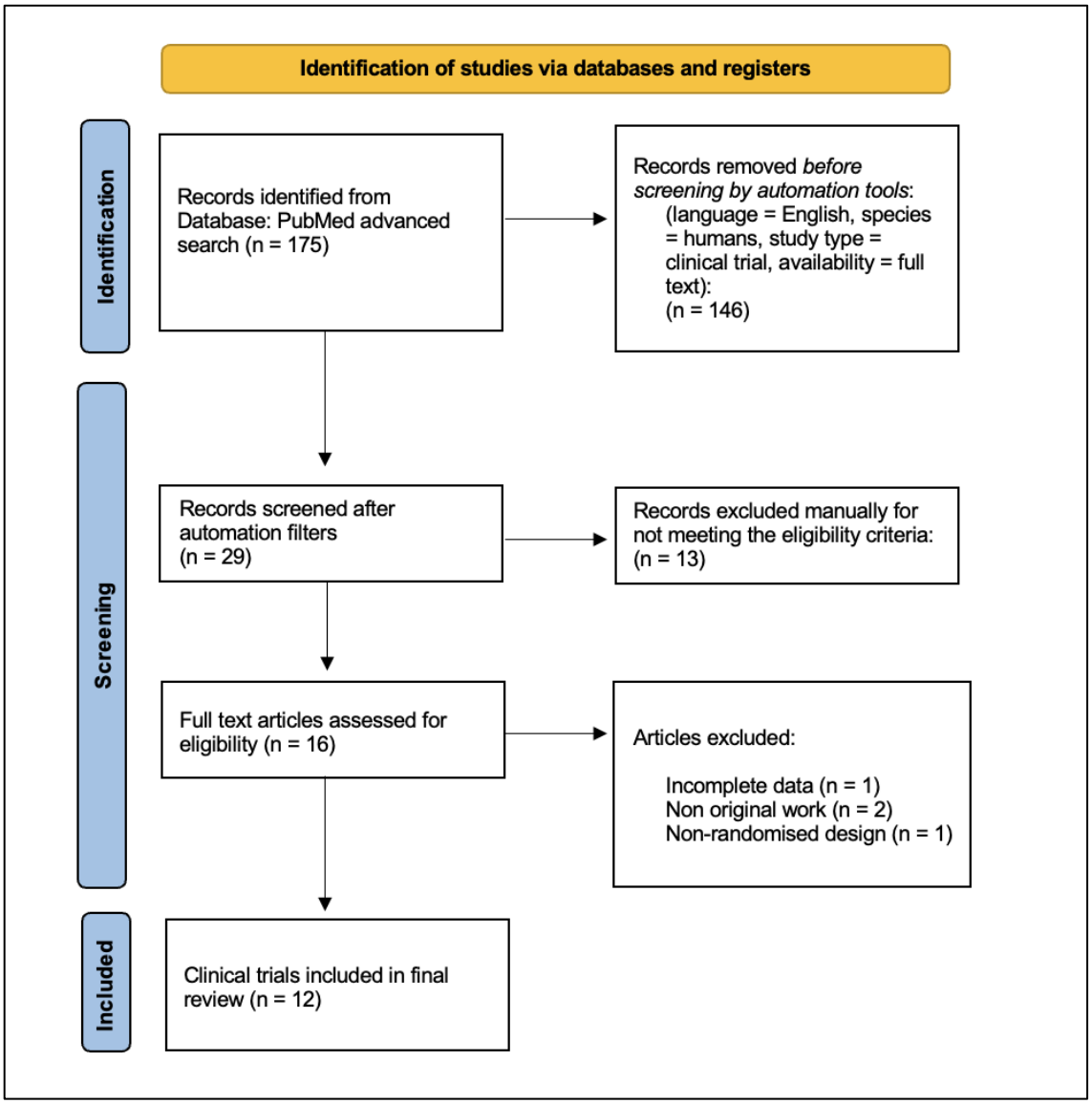
Study search and selection

A total of 175 records were initially identified through PubMed. The process of study selection, screening, and final inclusion/exclusion is summarised in Figure 2. An initial search of relevant databases on PubMed, from February 14, 2013, to August 2, 2025, using the term "Anifrolumab," yielded 338 articles. To refine the results, MeSH-based search filters were applied using MeSH-Tome advanced search. "Systemic Lupus Erythematosus (SLE)" as a MeSH term yielded 175 publications. Further limiting the search to clinical trials alone yielded 29 relevant studies. After screening titles and abstracts, 13 studies were excluded for failing to meet eligibility criteria, and 16 full-text articles were selected for detailed review.

Furthermore, four studies were excluded due to non-randomized design, incomplete data, and non-original work. A total of twelve clinical studies evaluating anifrolumab in patients with SLE were identified, encompassing randomized controlled trials (RCTs), long-term extension (LTE) studies, subgroup analyses, and open-label extensions. These studies consistently demonstrated the efficacy, safety, and long-term outcomes of anifrolumab in adults with moderate-to-severe SLE.

Figure 2

PRISMA Flowchart Showing Identification of Studies.



Study characteristics

A total of 12 clinical studies were included in this systematic review, spanning Phase 2b and Phase 3 randomized controlled trials (RCTs), long-term extension (LTE) studies, subgroup analyses, post-hoc analyses, open-label extensions, and a translation study (Table 1). Further, the LTE cohorts with several hundred participants detected long-term patterns, such as sustained steroid sparing and LLDAS attainment, that are not visible in single 52-week RCTs. This

variation in study design is necessary to enable a robust evaluation of both the short-term and long-term efficacy and safety of anifluromab.

Table 1

Summary Table of Study Characteristics.

Category	Study	Design
Pivotal RCTs	TULIP-2 (Morand et al., 2020)	Phase 3, randomized, double-blind, placebo-controlled
	TULIP-1 & TULIP-2 LTE (Kalunian et al., 2023)	Phase 3, randomized, double-blind, placebo-controlled, LTE
	MUSE (Furie et al., 2017)	Phase 2b, randomized, double-blind, placebo-controlled, dose-ranging
Long-term Extensions	TULIP-LTE PROs (Strand et al., 2025)	3-year, randomized, double-blind LTE with PRO focus (Phase 3 LTE of the 1-year TULIP-1 and TULIP-2 trials)
	MUSE Open-Label Extension(Chatham et al., 2021)	Phase 2, 3-year, multinational, open-label extension
Subgroup analyses	TULIP-LTE Japan subgroup (Tanaka et al., 2024)	Subgroup analysis of TULIP LTE
	TULIP-2 Japanese subanalysis (Tanaka et al., 2023)	Phase 3, Post hoc subgroup analysis of TULIP-2
	Japan Phase 2 open-label (Tanaka et al., 2020)	Multicenter, phase 2, open-label, dose-escalation
Post-Hoc Analyses	Concordance & discordance of SLE endpoints (Bruce et al., 2022)	Pooled analysis of MUSE, TULIP-1/2 (endpoint concordance)
	Flare analysis (Furie et al., 2021)	Pooled TULIP-1/2 (flare analysis)
	LLDAS & remission with anifrolumab (Morand et al., 2025)	Pooled TULIP-1/2 + LTE (disease activity/remission)
Translational	Type I IFN blockade (Baker et al., 2024)	Exploratory translational gene/proteomic study

Pivotal RCTs included the phase 3 TULIP-2 trial, a randomized, double-blind, placebo-controlled study that provided the primary evidence supporting anifrolumab efficacy (Morand et al., 2020). The TULIP-1 and TULIP-2 LTE further extended this program in phase 3, using a randomized, double-blind design (Kalunian et al., 2023). The earlier MUSE trial, a phase 2b dose-ranging RCT, provided the initial efficacy and safety data and informed subsequent trial designs (Furie et al., 2017). Long-term extension (LTE) studies assessed the durability of response and safety. The TULIP-LTE PROs reported outcomes from a 3-year, double-blind, LTE study focused on patient-reported outcomes (Strand et al., 2025). In contrast, the MUSE Open-Label Extension followed patients for three years in a multinational, open-label setting (Chatham et al., 2021).

Additionally, subgroup analyses examined regional and population-specific differences. These included the TULIP-LTE Japan subgroup and the TULIP-2 Japanese sub-analysis, both of which focused on Japanese patients(Tanaka et al., 2023, 2024), as well as the Japan Phase 2 open-label study, a multicenter, dose-escalation trial (Tanaka et al., 2020). Moreover, post hoc analyses examined secondary outcomes across pooled datasets. These included concordance and discordance of SLE endpoints, pooled flare analysis of TULIP-1/2, and pooled analyses assessing low disease activity and remission (Bruce et al., 2022; Furie et al., 2021; Morand et al., 2025). Finally, translational studies have investigated the mechanistic basis of treatment response, including an exploratory gene and proteomic study on type I IFN blockade (Baker et al., 2024). Together, the included studies spanned from early dose-ranging RCTs to multinational phase 3 programs, with subsequent extension and subgroup analyses, as well as translational investigations, providing a comprehensive evaluation of anifrolumab in SLE.

Population and treatment regimen

Across the 12 studies, the populations consisted of adults, typically 18-70 years old, with moderate-to-severe, predominantly seropositive SLE while consistently excluding patients with severe active lupus nephritis and active neuropsychiatric SLE (Table 2).

Table 2

Summary Table of Study Population and Anifluromab Regimen.

Category	Study	Population	Anifrolumab Regimen
Pivotal RCTs	TULIP-2 (Morand et al., 2020)	362 adults with moderate-to-severe active SLE (18–70 y), seropositive; no severe nephritis/NP-SLE	300 mg IV q4w × 48 w
	TULIP-1 & TULIP-2 LTE (Kalunian et al., 2023)	547 Adults with moderate to severe SLE who had completed either TULIP-1 or TULIP-2 trials and continued into this extension study. No severe active lupus nephritis	300 mg IV q4w (continued)
	MUSE (Furie et al., 2017)	305 adults (18–65 years) with active SLE on SOC	300 mg or 1000 mg IV q4w × 48 w
Long-term Extensions	TULIP-LTE PROs (Strand et al., 2025)	369 adults with moderate-to-severe active SLE	300 mg IV q4w up to 4 y
	MUSE Open-Label Extension(Chatham et al., 2021)	Adults with moderate-to-severe SLE who completed MUSE Phase IIb RCT Enrolled: 218/246 (88.6%) Completed 3 yrs: 139 (63.8%)	1000 mg IV q4w → 300 mg IV q4w
Subgroup analyses	TULIP-LTE Japan subgroup (Tanaka et al., 2024)	809 Japanese patients (18-70 years) entering LTE after TULIP	300 mg IV q4w
	TULIP-2 Japanese subanalysis (Tanaka et al., 2023)	362 adults with moderate-to-severe active SLE	300 mg IV q4w × 48 w
	Japan Phase 2 open-label (Tanaka et al., 2020)	20 Japanese patients (18-65 years) entering LTE after TULIP	300 mg IV q4w × 24 w (+ extension)
Post-Hoc Analyses	Concordance & discordance of SLE endpoints (Bruce et al., 2022)	Adults with moderate-to-severe SLE on standard therapy TULIP-1: 364 pts (Ani 180 / Pbo 184) TULIP-2: 362 pts (Ani 180 / Pbo 182) MUSE: 201 pts (Ani 99 / Pbo 102)	300 mg IV q4w (per parent trials)
	Flare analysis (Furie et al., 2021)	726 adults with moderate-to-severe active SLE	300 mg IV q4w × 48 w
	LLDAS & remission with anifrolumab (Morand et al., 2025)	369 adults with moderate-to-severe active SLE (18–70 y), continuing long term	300 mg IV q4w
Translational	Type I IFN blockade (Baker et al., 2024)	502 Patients with moderate-to-severe SLE from TULIP-1/2	300 mg IV q4w

The most widely used intervention with anifluromab across the 12 studies was a 300 mg intravenous dose every 4 weeks. The pivotal TULIP-2 trial (362 patients) tested anifrolumab 300 mg IV every 4 weeks (q4w) for 48 weeks (Morand et al., 2020). In the TULIP-1 & TULIP-2 LTE (547 patients), this regimen was continued for long-term follow-up (Kalunian et al., 2023). The MUSE phase 2b trial (305 patients) evaluated 300 mg or 1000 mg IV q4w for 48 weeks**,** with the subsequent MUSE open-label extension transitioning all patients to 300 mg IV q4w (Furie et al., 2017). Japanese subgroup studies, including the TULIP-LTE Japan subgroup (809 patients) and the TULIP-2 Japanese sub-analysis (362 patients), confirmed efficacy with the same 300 mg regimen (Tanaka et al., 2023, 2024). A smaller Phase 2 Japanese open-label study (20 patients) also used 300 mg IV q4w for 24 weeks with extension (Tanaka et al., 2020). Pooled post-hoc analyses across TULIP-1/2 and MUSE (encompassing up to 726 patients) consistently supported outcomes under the 300 mg IV q4w regimen (Furie et al., 2021).

Additional analyses explored long-term remission (Morand et al., 2025) and translational outcomes in 502 patients from TULIP-1/2 (Baker et al., 2024). Overall, the populations were representative of active SLE, and the treatment regimen was uniform, centered on anifrolumab 300 mg IV q4w plus standard-of-care therapy.

Efficacy outcomes

According to the 12 clinical studies, anifrolumab demonstrated consistent efficacy for improving disease in patients with moderate to severe SLE (Table 3).

In the TULIP-2 trial, the primary endpoint of BICLA response at week 52 was met, with remarkably higher response rates in the anifolumab group compared to the placebo group (47.8% vs. 31.5%; Δ 16.3%, 95% CI 6.3–26.3; $p = 0.001$) (Morand et al., 2020). Treatment benefits were also observed in IFN-high patients (48% vs. 30.7%) (Morand et al., 2020), and these benefits were extended to additional key outcomes, including improvements in skin outcomes (CLASI) and corticosteroid tapering (Furie et al., 2017; Kalunian et al., 2023; Tanaka et al., 2023). In addition, the long-term extension studies determined sustained disease control and durable efficacy over 3 years (Tanaka et al., 2024). With anifolumab treatment, patients exhibited improved BICLA responses, reduced flare rates, and greater glucocorticoid-sparing capacity. Further supportive evidence from the TULIP-LTE PROs and MUSE Open-Label Extension analyses indicated sustained and clinically meaningful improvements in patient-reported outcomes (PROs), including SF-36, EQ-5D, HAQ-DI, and FACIT-F, over 4 years (Chatham et al., 2021; Strand et al., 2025). These improvements paralleled long-term reductions in disease activity and glucocorticoid use, underscoring anifrolumab's benefits on health-related

quality of life. Moreover, subgroup analyses from Japanese cohorts also confirmed these findings, highlighting consistent efficacy with sustained reductions in SLEDAI scores, successful glucocorticoid tapering, and low flare rates over 3-4 years (Tanaka et al., 2020, 2023, 2024).

Table 3

Summary of Clinical Trials Evaluating Anifrolumab Efficacy in SLE.

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Category	Study	Primary End point	Primary results	Key secondary End points
Pivotal RCTs	TULIP-2 (Morand et al., 2020)	BICLA at week 52	47.8% vs 31.5% (Δ 16.3%, 95% CI 6.3–26.3; p=0.001)	IFN-high: 48.0% vs 30.7%; improved CLASI; more successful GC taper
	TULIP-1 & TULIP-2 LTE (Kalunian et al., 2023)	Long-term safety (EAIRs); sustained efficacy	Similar AE and SAE rates between anifrolumab and placebo; no new safety signals identified. Sustained disease control	PROs, CLASI, Sustained BICLA responses; reduced flare rates; GC sparing; more successful corticosteroid tapering
	MUSE (Furie et al., 2017)	SRI(4) at week 24 with OCS taper add-on	Primary narrowly missed; multiple secondary endpoints favored 300 mg	Higher BICLA, CLASI, joint improvements; IFN signature neutralization
Long-term Extensions	TULIP-LTE PROs (Strand et al., 2025)	Change in PROs (e.g., SF-36, FACIT-F, EQ-5D, HAQ-DI)	Sustained, clinically meaningful PRO improvements vs placebo. Both groups improved, but anifrolumab showed numerically greater improvement in bodily pain and mental health domains by wk 208	Sustained improvements in SF-6D and HRQoL, alongside ↓ disease activity and GC use
	MUSE Open-Label Extension(Chatham et al., 2021)	Long-term safety/tolerability	No new safety signals; 6.9% AE-related discontinuation; sustained activity improvements	Stable SDI; durable IFN-signature suppression; stable/improved HRQoL
Subgroup analyses	TULIP-LTE Japan subgroup (Tanaka et al., 2024)	Long-term safety and tolerability of anifrolumab 300 mg IV Q4W in Japanese pts with SLE over 4 yrs	AE and SAE rates similar between anifrolumab and PBO, no new safety signals	Sustained ↓ in SLEDAI, ↓ GC use, and stable low flare rate, mostly mild/moderate
	TULIP-2 Japanese subanalysis (Tanaka et al., 2023)	BICLA at week 52	Higher BICLA with anifrolumab vs placebo (directionally/statistically)	CLASI improvement; greater OCS taper success
	Japan Phase 2 open-label (Tanaka et al., 2020)	Safety/tolerability	No unexpected safety issues; clinical improvements seen	SLEDAI-2K, BILAG, CLASI improvements; steroid-sparing trends
Post-Hoc Analyses	Concordance & discordance of SLE endpoints (Bruce et al., 2022)	Concordance between BICLA and SRI(4)	~78–85% concordance; dual response favored anifrolumab	78–85% concordant (κ=0.6–0.7, p<0.001) Dual resp fav Ani in all 3 trials (p≤0.004) TULIP-1 discordant grp 11% (40/364), more placebo (28) vs Ani (12). Placebo pts had lower baseline disease activity, lower joint counts, ↑ glucocorticoid tapering, ↑ arthritis resp.
	Flare analysis (Furie et al., 2021)	Annualized flare rate (≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B); time to first flare	Ani ↓ flare rate vs Pbo (rate ratio 0.75; 95% CI 0.60–0.95) Longer time to 1st flare (HR 0.70; 95% CI 0.55–0.89) Fewer patients with ≥1 flare (Δ –9.3%) Fewer BICLA responders with ≥1 flare (21.1% vs 30.4%) In baseline GC ≥10 mg/day group: more remained flare-free with Ani (40.0% vs 17.3%)	Time to first flare; proportion of patients with ≥1 flare; organ-domain flares (musculoskeletal, mucocutaneous); flares in BICLA responders; flares in patients with sustained glucocorticoid taper. (All favored anifrolumab.)
	LLDAS & remission with anifrolumab (Morand et al., 2025)	LLDAS at 4 y; time in LLDAS; DORIS remission	After 4 years, significantly more anifrolumab patients reached **LLDAS** (36.9% vs 17.1%; OR 2.7; P=.0081) and a higher (though borderline) proportion reached **DORIS remission** (30.3% vs 18.3%; OR 1.9; P=.0663). Time to first LLDAS (HR 1.56, P=.0024) and first DORIS (HR 1.50, P=.0373) both favored anifrolumab. Anifrolumab patients also spent more time in LLDAS/DORIS over 4 years	Anifrolumab patients spent more time in LLDAS (13.9 vs 8.7 months; P=.0004) and DORIS (7.3 vs 3.5 months; P=.0032) than placebo, with higher proportions achieving ≥20%, ≥50%, and ≥70% time in these states (all P<.01). These benefits were linked to less damage accrual and reduced glucocorticoid use.
Translational	Type I IFN blockade (Baker et al., 2024)	Modulation of IFN-driven pathways; Gene and protein expression changes (transcriptome and plasma proteome)	It downregulated type-I and type-II IFN-induced pathways and type-III IFN-λ proteins, suppressed apoptotic and NETosis pathways, and reduced innate/inflammatory cytokines and B-cell cytokines.	increased T-cell/lymphocyte gene modules, decreased monocyte and plasma-cell modules; in silico cell deconvolution showed ↑ mucosal-associated invariant T and γδT cells and ↓ monocytes after treatment. Overall, broad IFN-driven inflammatory pathways were dampened.

A post hoc flare analysis showed that anifrolumab remarkably reduced flare frequency (rate ratio 0.75; 95% CI 0.60–0.95) and prolonged long-term flare-free survival (HR 0.70; 95% CI 0.55–0.89) (Furie et al., 2021). These effects were evident in patients with baseline glucocorticoid ≥10 mg/day, where 40% remained flare-free compared to the placebo group (17.3%) (Furie et al., 2021), and fewer BICLA responders subsequently experienced a flare (Furie et al., 2021). Lastly, the long-term control of the disease and remission endpoints were assessed via LLDAS (36.9% vs 17.1%; OR 2.7; p=.0081) and DORIS remission (30.3% vs 18.3%; OR 1.9; p=.0663) criteria, which displayed higher attainment rates along with longer duration of low disease activity and remission states in patients receiving anifrolumab (Morand et al., 2025). The translational analyses also showed suppression of type I IFN-driven inflammatory pathways and indicate clinical benefits, including reduced apoptotic and NETosis signatures (Table 3). This treatment downregulated IFB-driven and inflammatory cytokines and restored T-cell-associated gene expression (Baker et al., 2024), thereby contributing to the enhanced adaptive immune balance. Overall, these studies confirm that anifrolumab demonstrated robust, durable, and multidimensional efficacy across clinical, patient-reported, and biomarker endpoints, underscoring its role as a long-term therapy for SLE.

Safety and Adverse effects

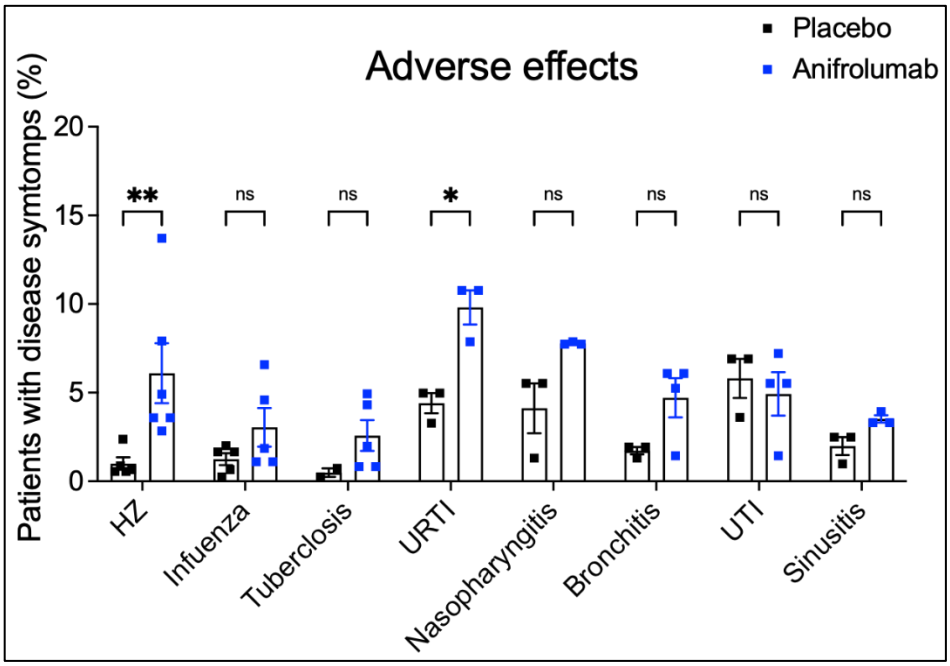
Anifluromab has demonstrated a consistent safety profile across all the studies. Common adverse events (AEs) included upper respiratory tract infections (URTI), nasopharyngitis, influenza, and an increased incidence of herpes zoster (HZ) compared with placebo (Furie et al., 2017; Morand et al., 2020; Tanaka et al., 2020, 2023), reflecting the immunomodulatory nature of anifrolumab's mechanism of action. While many studies reported a wide range of additional

AEs, including headache, fatigue, nausea, injection-site reactions, cough, pneumonia, arthralgia, and upper abdominal pain, these were not consistently present across all trials. The small open-label safety study (Tanaka et al., 2023) and subgroup LTEs (Tanaka et al., 2020, 2024) reported consistent tolerability and few severe HZ cases. The rate of serious adverse events (SAEs) was similar to placebo in long-term extension studies (LTEs) and the pooled analyses (Baker et al., 2024; Chatham et al., 2021; Kalunian et al., 2023; Strand et al., 2025; Tanaka et al., 2024). Moreover, no new or unexpected long-term safety signals emerged over the 4 years.

Notably, re-analysis of these published clinical trials showed that the incidence of most treatment-related adverse events was comparable between the anifrolumab and placebo groups (Figure 3). Across studies, influenza, tuberculosis, nasopharyngitis, bronchitis, urinary tract infection (UTI), and sinusitis occurred at similar frequencies (ns=not significant, $p>0.05$) (Figure 3). In contrast, HZ and URTI were reported more frequently among patients receiving anifrolumab compared to placebo groups ($p<0.05$) (Figure 3). Overall, the pooled re-analyzed data indicate that anifrolumab maintains an acceptable safety profile.

Figure 3

Adverse Effects of Anifrolumab Across Published Clinical Studies



Each dot represents an individual published study reporting the percentage of patients experiencing the indicated adverse events, including influenza, tuberculosis, upper respiratory tract infection (URTI), nasopharyngitis, bronchitis, urinary tract infection (UTI), and sinusitis. Bars show the mean proportion of affected patients (%) in the anifrolumab and placebo groups across all studies. Statistical significance between treatment groups, as reported in the respective publications, is indicated as * $P<0.05$, ** $P<0.01$; ns, not significant.

Discussion

Anifrolumab is a fully humanized monoclonal antibody that targets the type I interferon receptor (IFNAR1) and inhibits type I interferon (IFN)-mediated signaling pathways. Type I IFNs play a central role in the pathogenesis of SLE by regulating the survival, activation, and function of multiple immune cells, contributing to autoimmunity and tissue damage (Deeks, 2021). This systematic review integrated data from 12 clinical studies, including phase II and III

randomized controlled trials, long-term extension studies, open-label studies, post hoc/subgroup analyses, and translational studies, to evaluate the efficacy, safety, and clinical relevance of anifrolumab in moderate-to-severe SLE. This analysis demonstrated that anifrolumab provides sustained clinical benefits and consistently improves disease activity across multiple validated endpoints.

Despite the promising results, several limitations require consideration. Most trials excluded pediatric populations, patients with severe lupus nephritis and neuropsychiatric SLE, and severe comorbidities. This reduces the applicability of findings to broader patient populations. Some studies focused exclusively on specific populations, such as Japanese subgroups, which may reduce external validity or the relevance of the findings (Tanaka et al., 2020, 2023, 2024). Additionally, discordance between BICLA and SRI endpoints in specific trials complicates cross-study comparisons and underscores the need for standardized outcome measures (Bruce et al., 2022; Furie et al., 2017). The reliance on placebo comparators, rather than active comparators, leaves the comparative efficacy of anifrolumab with other biologics, such as belimumab, uncertain (Morand et al., 2020).

Compared with other approved monotherapies for SLE, such as belimumab, anifrolumab offers a distinct mechanism of action, targeting the type I interferon receptor rather than B-cell modulation. This may explain its more pronounced effects on skin and musculoskeletal manifestations, which are highly interferon-driven. However, while its efficacy in these domains appears promising, the broader clinical advantage over existing therapies remains context-dependent. Anifrolumab's infection-related safety profile, particularly its association with herpes

zoster and respiratory infections, should also be considered when evaluating against other biologics.

While long-term extension studies suggest sustained efficacy and disease control, durability should be interpreted as likely rather than definitively established (Chatham et al., 2021; Morand et al., 2025; Strand et al., 2025). Furthermore, the consistent signal for herpes zoster underscores the importance of pre-treatment vaccination strategies and vigilant monitoring for infections throughout aniflorumab therapy (Kalunian et al., 2023; Strand et al., 2025; Tanaka et al., 2020). Additionally, while anifrolumab demonstrates consistent efficacy at the 300 mg IV dose, dose-ranging studies suggest that higher doses do not necessarily confer additional benefit and may increase the risk of infections (Chatham et al., 2021; Furie et al., 2017). Further, rare or delayed adverse events may only emerge with broader clinical use, which emphasizes the need for ongoing post-marketing surveillance.

Future research should address these gaps by including patients with severe organ involvement, neuropsychiatric manifestations, and pediatric SLE, as well as ethnically diverse populations, to improve applicability. Investigating combination strategies with other immunomodulators may further enhance clinical outcomes. The wide age range of 18-70 years introduces potential variability in immune responsiveness, comorbidities, and drug metabolism, which could influence both efficacy and tolerability. Younger patients may exhibit stronger immunomodulatory responses, whereas older individuals could be more susceptible to infection-related adverse events. Additional studies should continue to explore biomarker-guided strategies, such as IFN signature stratification, to identify patients most likely to benefit. Although the current evidence overall supports anifrolumab as a safe and effective therapeutic

option, these approaches will strengthen the evidence base and optimize its clinical utility in SLE management.

Conclusion

Across 12 clinical studies, evidence converges to support the use of anifrolumab (300 mg IV every 4 weeks), which improves clinically meaningful outcomes in adults with moderate-to-severe SLE. Treatment with anifrolumab leads to consistent reductions in disease activity and flare rates, steroid-sparing effects, and sustained improvements in patient-reported outcomes over periods up to 4 years. The safety profile is acceptable and stable over time, with herpes zoster as the principal adverse signal. The totality of randomized trials and LTE evidence supports anifrolumab as a disease-modifying therapeutic option for the studied population while highlighting essential gaps for future research.

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