Concise Report

Real-world use of anifrolumab in systemic lupus erythematosus: A retrospective study from a Danish tertiary center (2022–2025)

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Abstract

Objective: To evaluate the real-world safety, efficacy, and steroid-sparing effects of anifrolumab in patients with systemic lupus erythematosus (SLE) treated at a tertiary referral center in Denmark.

Methods: We conducted a retrospective observational study of all SLE/discoid lupus patients who received at least one infusion of anifrolumab between May 2022 and February 2025 at Aarhus University Hospital. Clinical and laboratory data were extracted from electronic medical records at baseline, 3 months, 6 months, and last follow-up. Disease activity was assessed using SLEDAI-2K, Physician's Global Assessment (PGA), LLDAS, and DORIS criteria.

Results: Thirty-six patients (94% female, mean age 52 years) received anifrolumab for a mean of 462 days. Median SLEDAI-2K decreased from 8 at baseline to 2 at month 3, and to 0 at both month 6 and last follow-up. The proportion achieving SLEDAI-2K = 0 increased from 0% at baseline to 52% at both 6 months and last follow-up. At the last follow-up, 87% achieved both PGA ≤0.5 and LLDAS, while 70% achieved DORIS remission. Prednisolone doses declined by >50%. Skin and musculoskeletal involvement showed the greatest improvement. Herpesvirus-related infections were the most frequent adverse events; two severe cases occurred, though treatment was generally continued.

Conclusion: Anifrolumab was associated with rapid, sustained disease control and significant steroid-sparing effects. Herpesvirus infections were common, underscoring the importance of vaccination prior to treatment initiation. These findings support anifrolumab as an effective therapeutic option for SLE in routine clinical care.

Keywords

systemic lupus erythematosus, anifrolumab, real-world evidence, corticosteroids, remission, LLDAS

Introduction

Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disease characterized by diverse clinical manifestations, cumulative organ damage, and significant comorbidities.[1] SLE has a prevalence of 45 per 100,000 in Denmark; it predominantly affects women, typically diagnosed during their childbearing years.[2] SLE can involve virtually any organ system. Common manifestations include cutaneous lesions, arthritis, glomerulonephritis, and cardiovascular complications.[3]

Standard therapy follows the European Alliance of Associations for Rheumatology (EULAR) 2023 recommendations, centered on immunosuppressive agents such as hydroxychloroquine and low-dose glucocorticoids.[4] A treat-to-target approach is emphasized, aiming for Lupus Low Disease Activity State (LLDAS) or remission criteria in SLE (DORIS) as optimal outcomes.[5,6] Achieving these targets is associated with improved long-term prognosis and reduced organ damage in SLE.[7]

Anifrolumab is a fully human monoclonal antibody that binds the interferon (IFN)-α/β receptor subunit 1 (IFNAR1), thereby inhibiting the type I IFN (INF-I) pathway, which is central to SLE pathogenesis.[8] Anifrolumab reduces SLE disease activity and flares in many patients by suppressing

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IFN-I-driven inflammatory gene expression and downstream immune activation.[9] The European Medicines Agency (EMA) approved anifrolumab in 2022 as an add-on therapy for moderate-to-severe SLE, based on the Phase III trial (TULIP-2) demonstrating clinical efficacy in active SLE disease.[10] Post-hoc analyses of the TULIP trials further showed that anifrolumab-treated patients were more likely to achieve sustained LLDAS or remission over long-term follow-up than those on standard care alone.[11]

Anifrolumab has an acceptable safety profile in clinical trials.[10,12,13] The most common adverse events (AEs) include upper respiratory tract infections, infusion-related reactions, and herpes zoster reactivation. In the phase II/III program, 6.1% of patients on anifrolumab developed herpes zoster (HZ) versus ~1.3% on placebo, reflecting an exposure-adjusted risk difference of ~5.4% in the first year.[14] Nonetheless, real-world data on anifrolumab remain limited.[15,16,17,18] Most evidence to date comes from controlled trials in highly selected patients, and there is a need to understand its effectiveness and safety in routine clinical practice. In particular, data on sustained disease control, steroid-sparing effects, and uncommon adverse events in broader SLE populations are scarce.

This study reports real-world experience with anifrolumab in a Danish SLE group. We describe the efficacy of anifrolumab in achieving low disease activity/remission and reducing glucocorticoid use, as well as its safety profile in a tertiary care setting. We also highlight management considerations such as pre-treatment zoster vaccination and antiviral prophylaxis, given the prominence of herpesvirus-related AEs.

Methods

Study design

We conducted a retrospective observational study of SLE patients treated with anifrolumab at the Department of Rheumatology, Aarhus University Hospital (Denmark). All patients who received their first anifrolumab infusion between May 2022 and February 2025 were eligible. Inclusion criteria were: a clinical diagnosis of SLE (or discoid lupus), age ≥18 years, initiation of anifrolumab per the approved indication (moderate-to-severe SLE refractory to standard therapy), and residency in Denmark. Patients were identified via electronic medical records (EMRs) and included regardless of prior treatments or comorbidities. This study was approved as a quality improvement project. Since no biological samples were collected and data were obtained from routine care records, formal ethical committee approval was waived in accordance with Danish regulations and the Declaration of Helsinki.

Data collection

Clinical data were extracted from EMRs to a secure RedCap database (Redcap.au.dk). Baseline was defined as the date of the first anifrolumab infusion. Follow-up assessments were recorded, if available, at approximately 3 months, 6 months, and at the last available follow-up visit (defined as the final infusion prior to data cut-off or the visit at treatment discontinuation). Variables were collected from the clinical visit/blood sample closest to the corresponding assessment (for baseline assessment, provided that the visit occurred before infusion) and included patient demographics, disease duration, prior SLE therapies, SLE disease activity indices, laboratory parameters, concomitant medications, and adverse events. Disease activity was evaluated using the SLE Disease Activity Index 2000 (SLEDAI-2K) and Physician's Global Assessment (PGA, 0–3 scale). We also determined whether patients met criteria for LLDAS or DORIS remission at each time point. LLDAS was defined according to Franklyn et al. (SLEDAI-2K ≤4, no major organ involvement, no new disease activity, PGA ≤1, prednisolone ≤7.5 mg/day, and standard immunosuppressive dosing). DORIS remission was defined per the 2021 international task force guidelines (clinical SLEDAI = 0, immunosuppressives allowed, serology irrespective).

Data analysis

Descriptive statistics were used to summarize patient characteristics and outcomes. Continuous variables are presented as mean (standard deviation [SD]) or median [Range] as appropriate. Categorical variables are reported as frequencies and percentages. Changes in disease activity measures and laboratory values over time were assessed descriptively due to the limited sample size. The primary efficacy endpoints were the proportion of patients achieving LLDAS and remission on anifrolumab. Secondary endpoints included reduction in SLEDAI-2K scores, improvement in PGA, and glucocorticoid sparing (proportion of patients on prednisone and mean prednisone dose over time). Safety analyses focused on the incidence of adverse events, with particular attention to infections. Given the retrospective design, no formal hypothesis testing was performed. Data management and basic statistical analyses were performed using Microsoft Excel and R (v4.0) software.

Results

Patient characteristics

Between May 2022 and February 2025, 36 SLE patients were treated at our center and included in this study. The

Table 1. Baseline demographic and clinical characteristics of patients treated with anifrolumab (N = 36).

	N = 36
Demographics and clinical characteristics	
Age (years): Mean (SD)	52 (17.2)
Gender: Female, n (%)	34 (94,4%)
Years since diagnosis: Mean (SD)	14 (4.8)
SLEDAI-2K score median [range]	8 [2-20]
SLEDAI 2K	
No activity (SLEDAI = 0), n (%)	0 (0)
Mild activity (SLEDAI = 1–5), n (%)	8 (22)
Moderate activity (SLEDAI = 6–10), n (%)	16 (44)
High activity (SLEDAI = 11–19), n (%)	11 (31)
Very high activity (SLEDAI ≥ 20), n (%)	1 (3)
Medication	
Prior biologic use	
None n (%)	16 (44)
Belimumab n (%)	11 (31)
Rituximab n (%)	10 (28)
Other biologic treatment n (%)	4 (11)
Days on anifrolumab, mean (SD)	461.5 (345.8)
Concomitant SLE medication	
Hydroxychloroquine n (%)	26 (72)
Prednisolone n (%)	21 (58)
Mycophenolate n (%)	8 (22)
Azathioprine n (%)	5 (14)
Tacrolimus n (%)	2 (6)
Methotrexate n (%)	1 (3)
Immunoglobuline n (%)	0 (0)
Leflunomide n (%)	0 (0)
Cyclophosphamide n (%)	0 (0)
Salazopurine n (%)	0 (0)
Zoster vaccination prior to anifrolumab treatment	
Not vaccinated n (%)	26 (72.2)
Vaccinated, 1 dose n (%)	7 (19.4)
Vaccinated, 2 doses n (%)	3 (8.3)

Values are presented as mean (SD) or n (%), unless otherwise indicated. Disease activity was assessed using the SLE Disease Activity Index 2000 (SLEDAI-2K). SLEDAI-2 K categories: mild 1–5, moderate 6–10, high 11–19, very high ≥20. Prior biologic treatment refers to any previous exposure before anifrolumab initiation. Concomitant SLE medication was recorded at the time of the first anifrolumab infusion. Zoster vaccination refers to receipt of the recombinant zoster vaccine (Shingrix) before starting anifrolumab.
Abbreviations: SLE, systemic lupus erythematosus; SD, standard deviation.

baseline demographic and clinical features are summarized in Table 1. Patients were predominantly female (94%) with a mean age of 52 years (±17). The mean disease duration at anifrolumab initiation was 14 (±4.8) years. Concomitant therapy at baseline reflected standard SLE management (Table 1). Nearly half of the patients (44%) were biologic-naïve, while others had prior exposure to belimumab (31%) and/or rituximab (28%). Hydroxychloroquine was being used by 72% of patients. More than half (58%) were receiving oral prednisolone (median dose ~5–7.5 mg daily), and 14% were on a medium dose (≥7.5 mg/day). Concurrent conventional immunosuppressants included mycophenolate mofetil (22%), azathioprine (14%), tacrolimus (6%), and methotrexate (3%). No patients were on cyclophosphamide or IVIG at baseline. All patients had active or refractory disease despite standard of care at the time of anifrolumab initiation.

Baseline SLEDAI-2K scores ranged from 2 to 20, with a median of 8, indicating moderate disease activity on average. In fact, 75% of patients had moderate or high disease activity (SLEDAI ≥6) at baseline; only 22% had mild activity (SLEDAI 1–5), and none were in clinical remission (SLEDAI 0) (Table 1). The most common active disease manifestations at baseline were mucocutaneous and musculoskeletal involvement: 33 patients (92%) had active skin lupus (rash and/or alopecia), and 17 (47%) had active arthritis or arthralgias. Other organ systems involved at baseline included hematologic cytopenias in 5 patients (14%) and low-grade renal or serositis involvement in a minority (<10%).

At baseline, 72% were unvaccinated against herpes zoster; 8% had completed the vaccine series, and 19% had received 1 dose of the recombinant vaccine (Table 1). During follow-up, 11 previously unvaccinated patients completed 2 doses, 4 completed a second dose, and 2 received 1 dose. Thirteen patients remained entirely unvaccinated.

Treatment exposure and discontinuation

The 36 patients were followed for a mean anifrolumab exposure time of 462 days (approximately 15 months) (Table 1). By the data cut-off (February 2025), 30 patients (83%) remained on anifrolumab therapy. Six patients (17%) had discontinued treatment: four due to adverse events (detailed below) and two because they had achieved sustained remission, and they/their physicians elected to stop therapy. An additional 4 patients had a temporary treatment pause (defined as > 2 months) but later resumed anifrolumab. Reasons for treatment pause included personal considerations, such as pregnancy wishes, achievement of disease remission, or aimed at using the minimal necessary medication. Figure 1 summarizes patient exposure to anifrolumab during the study period. Drug retention at 12 months was 89%, comparable to real-world registry data.[18]

Adverse events

Overall, 14 patients (39%) experienced ≥1 AE, mostly mild-to-moderate (See Supplemental Material). Herpesvirus infections were most frequent (56%). Five patients (14%) developed herpes zoster, including one case of varicella zoster virus encephalitis requiring

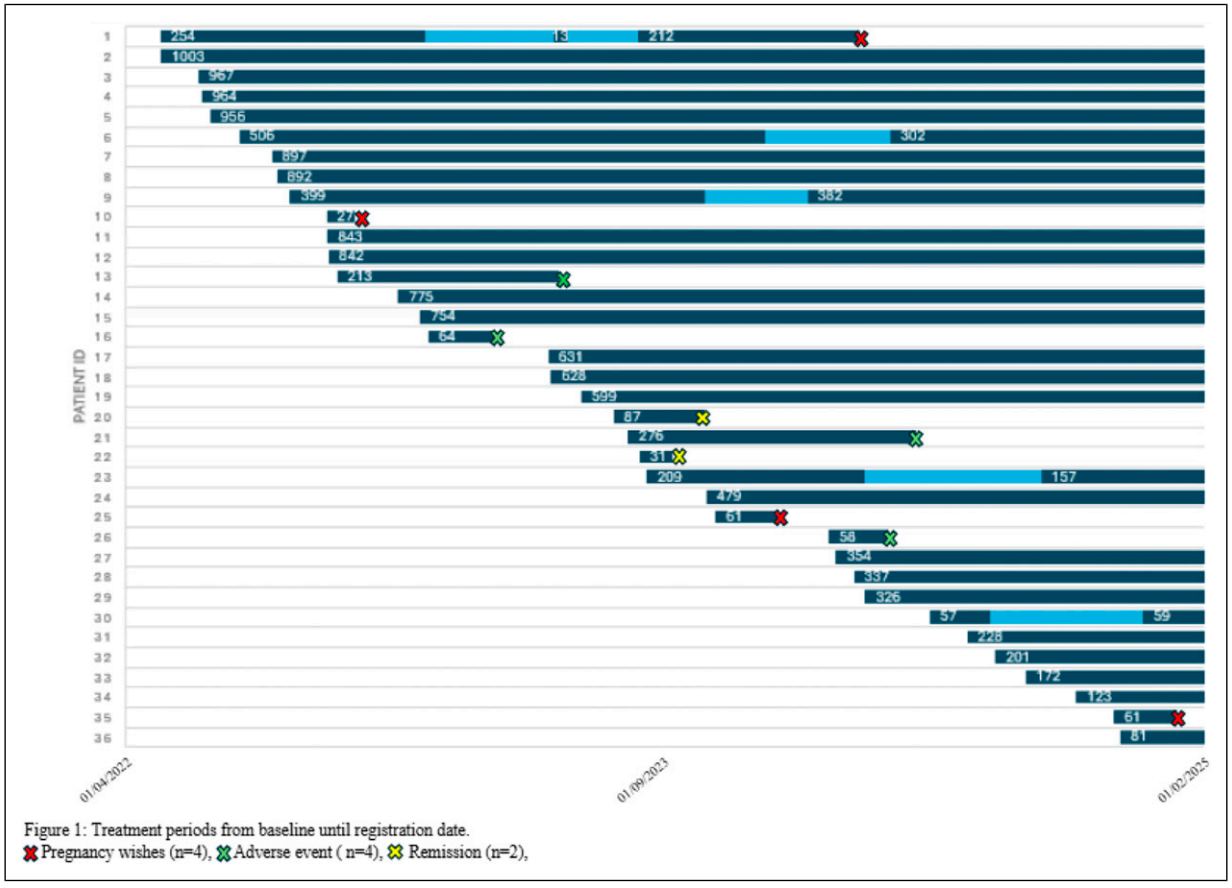

Figure 1. Treatment exposure and patient disposition during anifrolumab therapy, summarizing anifrolumab treatment duration, discontinuations, and temporary treatment pauses among the 36 patients. The numbers in the bars indicate treatment days. Reasons for permanent discontinuation include pregnancy wish (✖, n = 4), adverse events (✖, n = 4), and sustained remission (✖, n = 2). A treatment pause was defined as a break of more than two scheduled infusions; some patients who paused because of remission later experienced flares and restarted anifrolumab.

hospitalization.[19] The patient recovered and, after receiving the recombinant zoster vaccine, chose to resume anifrolumab due to its therapeutic benefit. Another patient developed a disseminated herpes simplex virus (HSV-2) infection (widespread mucocutaneous HSV lesions), leading to permanent discontinuation of anifrolumab.[19] In addition, two patients had recurrent oral HSV-1 flares, and one had genital herpes; all three were managed with antivirals without stopping anifrolumab. Notably, among the six patients with zoster manifestations, only two had been vaccinated against zoster prior to therapy (one with a single dose, one with two doses). Other infections, apart from herpesviruses, were rare. Two patients developed upper respiratory tract infections (sinusitis/bronchitis) during treatment.

Five non-infectious AEs were also recorded. First, one patient experienced a serum sickness-like reaction (transient illness with fever, rash, and arthritis), and the therapy was subsequently discontinued. Secondly, two patients experienced ischemic strokes, which were attributed to comorbidities including antiphospholipid antibodies, hypertension, active smoking, high age, and active lupus. One patient decided to discontinue treatment after the stroke event. Finally, two patients reported minor AEs: restless legs syndrome and infusion-related episodic periorbital edema and chills. These events did not lead to treatment discontinuation. Importantly, no deaths occurred.

Disease activity and remission

Disease activity improved rapidly. Median SLEDAI-2K fell from 8 at baseline to 2 at 3 months and to 0 by 6 months, remaining at 0 at last follow-up (Table 2). The proportion with moderate-to-high activity declined from 75% at baseline to 7% at 3 months, and high activity (SLEDAI ≥11) fell from 34% to 0% at all subsequent visits.

Treat-to-target outcomes improved substantially (Figure 2). At 3 months, 83% achieved LLDAS and 55% DORIS clinical remission. At last follow-up, 87% met LLDAS and 70% DORIS

Table 2. Disease activity response during anifrolumab treatment.

Response	Baseline N = 36	Month 3 N = 29	Month 6 N = 27	Last follow-up N = 23
SLEDAI-2K score, median [range]	8 [2–20]	2 [0–8]	0 [0–8]	0 [0–10]
No activity (SLEDAI = 0), n (%)	0 (0)	12 (41)	14 (52)	12 (52)
Mild activity (SLEDAI = 1–5), n (%)	8 (22)	15 (52)	9 (33)	10 (43)
Moderate activity (SLEDAI = 6–10), n (%)	16 (44)	2 (7)	4 (15)	1 (4)
High activity (SLEDAI = 11–19), n (%)	11 (31)	0 (0)	0 (0)	0 (0)
Very high activity (SLEDAI ≥ 20), n (%)	1 (3)	0 (0)	0 (0)	0 (0)
PGA score, median [range]		0 [0–2]	0 [0–1]	0 [0–1]
0<0.5, n (%)		17 (59)	19 (70)	20 (87)
0.5<1, n (%)		5 (17)	3 (11)	3 (13)
1.0<2.0, n (%)		6 (21)	5 (19)	0 (0)
2.0–3.0, n (%)		1 (3)	0 (0)	0 (0)

SLE disease activity at baseline and during follow-up. Values are given as median [Range] or n (%). SLEDAI-2 K categories: no activity (0), mild, 1–5 moderate, 6–10 high, 11–19 very high (≥20). Physician's Global Assessment (PGA) was scored on a 0–3 visual analogue scale. PGA categories are shown as the proportion of patients within each PGA range at the specified visit. Numbers at each time point reflect available data: baseline N = 36, month 3 N = 29, month 6 N = 27, last follow-up N = 23.
Abbreviations: SLEDAI-2K, SLE Disease Activity Index 2000; PGA, Physician's Global Assessment.

criteria. Non-responders had either discontinued early due to AEs or had refractory damage-related disease. Overall, remission rates were comparable to or exceeded those reported in clinical trials.[11,15,16,18]

Organ involvement

Figure 3 illustrates the trajectory of organ-specific disease involvement over time, according to the SLEDAI-2K score. The strongest improvements were seen in the mucocutaneous and musculoskeletal domains. Of the 33 patients with active skin lupus at baseline, only 5 still had active skin activity by the 3-month visit. Likewise, the number of patients with active musculoskeletal involvement declined from 17 at baseline to 3 at 3 months follow-up. These improvements were largely maintained during follow-up. Hematological activity resolved in all 5 patients by the 3-month follow-up and remained largely quiescent. By the last

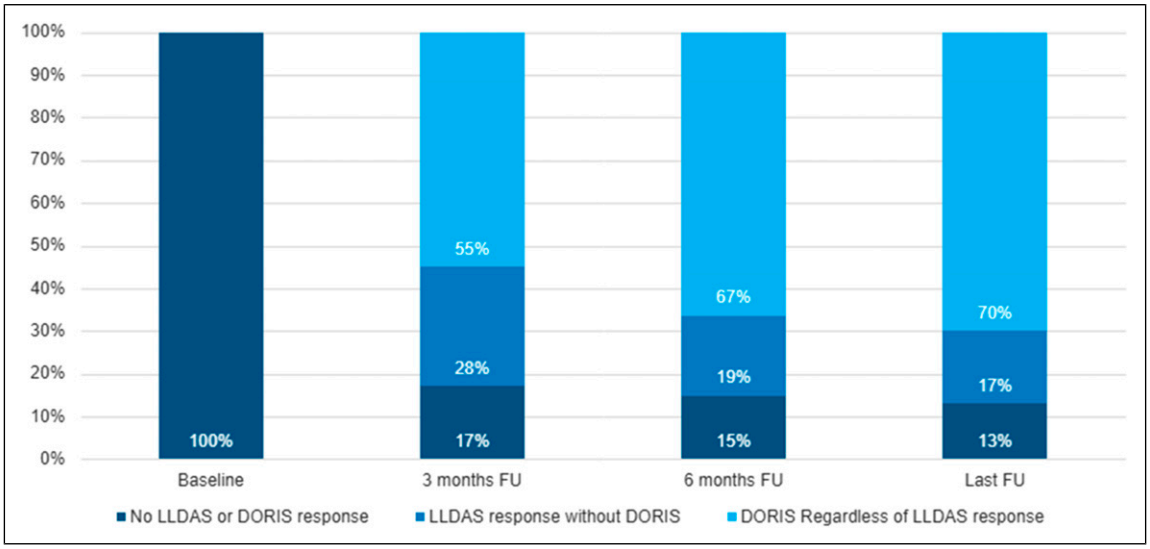

Figure 2. Attainment of LLDAS and DORIS during anifrolumab treatment. Proportion of patients achieving LLDAS and DORIS at 3 months, 6 months, and the last follow-up. Bars represent the percentage of evaluable patients meeting each outcome at the specified time point. LLDAS and DORIS were defined according to published criteria, incorporating SLEDAI-2K, PGA, and glucocorticoid dose thresholds. Nearly all patients reached LLDAS, and a high proportion achieved DORIS with continued anifrolumab therapy.
Abbreviations: LLDAS, lupus low disease activity state; DORIS, definition Of Remission In SLE; PGA, Physician's Global Assessment; SLEDAI-2K, SLE Disease Activity Index 2000.

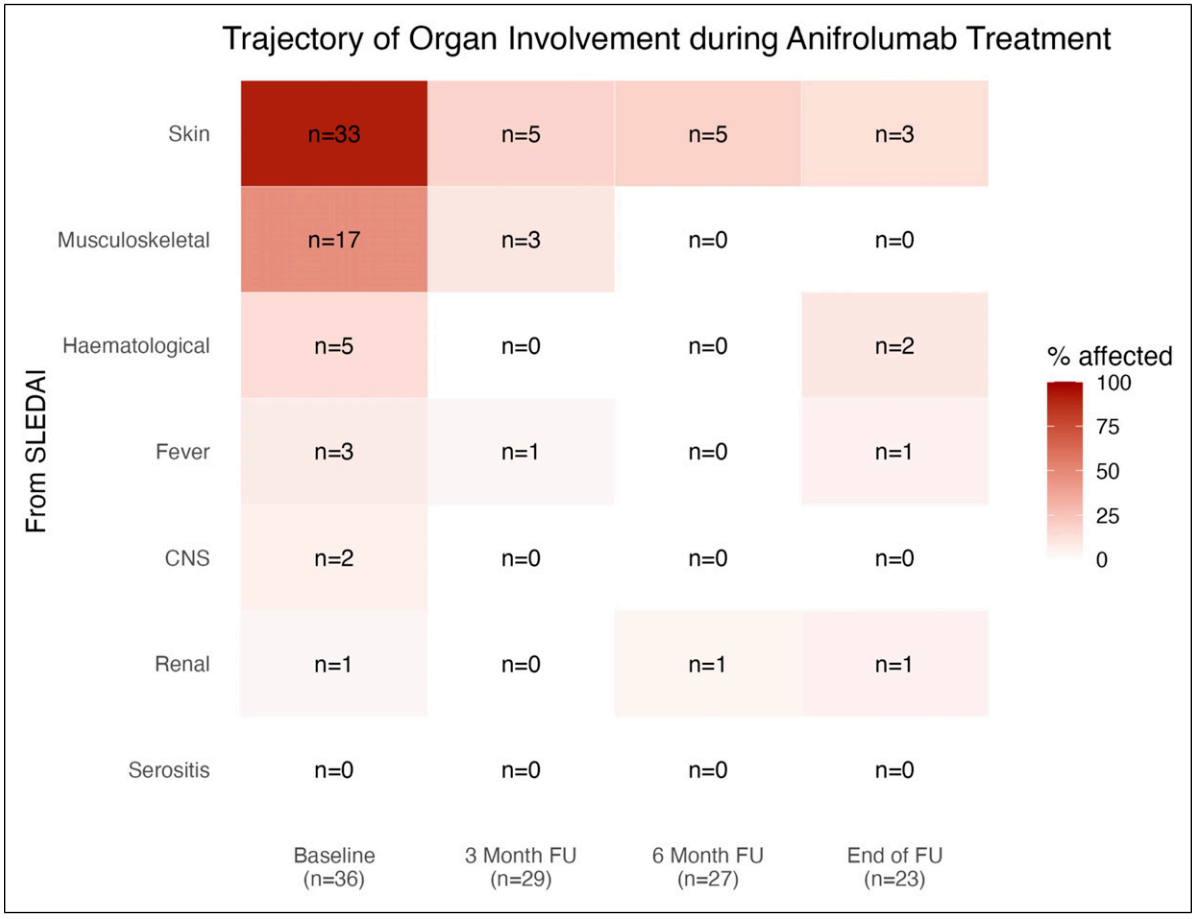

Figure 3. Trajectory of organ involvement during anifrolumab treatment. Heatmap showing the proportion of patients with active disease in each Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) organ domain at baseline, 3 months, 6 months, and last follow-up. Color intensity reflects the percentage of patients with active involvement in a given domain at each time point (see color scale), and the numbers within each cell indicate the absolute number of affected patients (n). The mucocutaneous and musculoskeletal domains were the most frequently active at baseline and showed marked improvement after initiation of anifrolumab. Abbreviations: CNS, central nervous system; FU, follow-up.

follow-up, 2 patients had a recurrence of mild cytopenias. Other organ systems, such as renal and CNS involvement, were infrequent in this study group; those with low-grade proteinuria or a history of nephritis did not experience renal flare with anifrolumab, and no new major organ involvement occurred.

Laboratory measurements

Mean anti-double-stranded DNA (dsDNA) antibody titers declined after treatment initiation, although normalization was uncommon. Complement responses were modest; C3 increased in some cases, whereas C4 levels remained largely unchanged. Lymphocyte counts rose from a mean of $0.9 \times 10^{\wedge} 9$/L at baseline to $1.4 \times 10^{\wedge} 9$/L at 3 months and subsequently remained within the normal Range. Overall, biochemical changes were consistent with a beneficial immunological effect, though full serologic remission (i.e., complete normalization of autoantibody and complement levels) was not routinely achieved. See Supplemental Material for graphic illustration of laboratory measurements.

Glucocorticoid use

Anifrolumab demonstrated a significant steroid-sparing effect (Figure 4). Prednisone use decreased from 58% at baseline to 35% at last follow-up, with a >50% reduction in mean daily dose. The proportion of patients on medium-dose prednisone (7.5–10 mg/day) dropped from 14% at baseline to 4% at last follow-up. No patients required high-dose prednisone (>10 mg/day) at the conclusion of the study. Patients who were steroid-free at baseline mostly remained so, and disease flares were generally managed without increasing corticosteroid doses. We did not observe an increased risk of AEs or infections among patients who were on prednisolone. Of the nine infection-related AEs, five occurred in patients who were not exposed to prednisone at

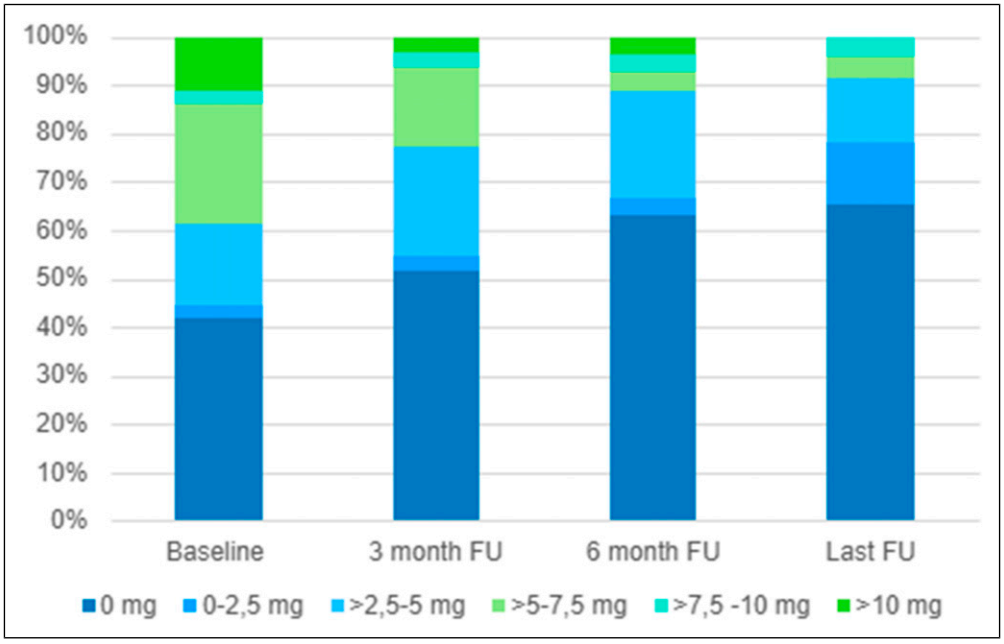

Figure 4. Oral glucocorticoid use before and during anifrolumab treatment. Distribution of daily prednisolone doses at baseline, 3 months, 6 months, and last follow-up (FU). Bars indicate the proportion of patients receiving no glucocorticoids, low-dose prednisolone (<7.5 mg/day), and medium-dose prednisolone (7.5–10 mg/day). A marked reduction in both the proportion of patients on prednisolone and the prescribed doses is seen over time. At the 3-month time point, data were available for 31 patients because some had laboratory and medication follow-up without an in-person visit.

any point during the study, one patient was receiving <5 mg/day, and three patients were on ≥7.5 mg/day at baseline.

Discussion

In this real-world Danish study of SLE, anifrolumab therapy led to rapid and sustained disease improvement, with the majority of patients achieving low disease activity or remission. These findings corroborate and extend the efficacy signals observed in clinical trials, while also providing insight into safety and management considerations in routine practice.

Our data show significant improvements in SLEDAI-2K score, PGA, and key organ manifestations shortly after treatment initiation, particularly in mucocutaneous and musculoskeletal disease - consistent with the interferon-driven pathogenesis of these domains. Nearly 90% achieved low disease activity, and ~70% complete clinical remission. For comparison, an Italian multicenter study of 26 refractory SLE patients reported 80% LLDAS and 50% remission at 6 months on anifrolumab.[16] TULIP trials reported ~37% LLDAS and 30% remission at 4 years with anifrolumab (versus 17% and 18% on placebo).[11] Likewise, the Japanese LOOPS registry analysis found that anifrolumab was effective even in patients with high disease activity who had failed multiple prior treatments, with high drug retention and sustained improvement over 12 months.[18] The high remission rates likely reflect phenotype-driven patient selection and close monitoring in our tertiary center, introducing selection bias but mirroring real-world prescribing practice for refractory disease.

One of the major goals in SLE management and treating to target is to minimize chronic glucocorticoid exposure due to its well-known toxicity. Even long-term low-dose prednisone (≤7.5 mg daily) is associated with significantly increased risks of organ damage, infection, osteoporosis, and metabolic complications.[20] In our patients, anifrolumab use was associated with a substantial reduction in steroid requirements, the mean prednisone dose more than halved, and many patients were able to discontinue steroids entirely. Flares were often managed by optimizing immunosuppressive therapy or maintaining timely anifrolumab dosing. It resonates with findings from both clinical trials and real-world practice.[18,21]

Importantly, our study also suggests a potentially novel insight. Glucocorticoids in SLE are traditionally introduced as bridging therapy because most immunosuppressive agents require 3–6 months to take full effect. In contrast, many patients receiving anifrolumab experienced a marked clinical improvement within the first month, indicating a considerably faster onset of action. This raises the possibility that anifrolumab could reduce or even replace traditional steroid-bridging strategies in selected patients; an important but still speculative paradigm shift requiring prospective validation.

Cutaneous improvement was particularly notable after anifrolumab initiation. In our cohort, 92% of patients had skin involvement captured by the SLEDAI rash domain at baseline, which decreased to 13% at 3 months. In our clinical practice, the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI-A and CLASI-D) is not routinely used; therefore, these specific data were not available for this analysis, despite CLASI scoring having been applied in the anifrolumab trials. Nevertheless, patient-reported outcomes from the PETUNIA study,[22] which included the first 14 patients treated with anifrolumab at our center, support the observed improvement in skin disease. In PETUNIA, the bothersomeness of skin involvement decreased from an average score of 8 before treatment to 1 following treatment. Although these patient-reported measures do not permit direct comparison with CLASI outcomes, they align with our SLEDAI-based findings and further support the positive impact of anifrolumab on cutaneous lupus activity.

Serologic responses were modest. We observed trends of decreasing anti-dsDNA titers and slightly rising complement C3 levels. By contrast, C4 levels remained unchanged, and many patients had persistently low-titer autoantibodies despite clinical remission. A recent systematic review by Mahmoud et al. similarly noted that anifrolumab tends to improve serologic activity (including dsDNA and C3) without fully normalizing these parameters.[23]

The discrepancy between serologic and clinical remission underscores that clinical indices should drive treatment decisions, and low-level serological activity in an otherwise controlled patient might be acceptable. Interestingly, we saw a rise in lymphocyte counts with anifrolumab, consistent with mitigation of IFN-induced lymphopenia.

The safety profile was largely favorable, with no new safety signals beyond those reported in clinical trials. The most common AEs were mild viral infections, particularly herpesvirus reactivations, which is biologically plausible given IFN-I inhibition. The incidence of herpes zoster (5 of 36 patients, ~14% over an average follow-up of ~1 year) exceeded that reported in the 52-week clinical trials (~6% on anifrolumab). Yet, all but one case were uncomplicated and manageable. The higher zoster rate may at least in part be attributable to the older mean age in our patient group (~52 years) compared with the mean age in the TULIP trial populations (~42 years). Age is well recognized as the strongest risk factor for herpes zoster.[24] Crucially, we documented two severe herpesvirus-related AEs. A disseminated HSV-2 infection and a case of VZV encephalitis, which to our knowledge have not been reported in anifrolumab-treated patients previously. Both cases have been reported in detail earlier.[19] Briefly, the patient with disseminated HSV-2 infection had no identifiable immunodeficiency on whole-genome sequencing and likely HSV-2 exposure 3 weeks before symptom onset. Importantly, this patient was not receiving prednisolone at the time of infection. The patient with VZV-encephalitis had a prior history of herpes zoster, age above 50 years, was receiving 10 mg/day of prednisolone at the time of infection, and had not received zoster vaccination prior to anifrolumab initiation.[19] Our findings reinforce that while most viral infections on anifrolumab are cutaneous and mild, severe disseminated herpesvirus infections can occur in susceptible individuals. We did not observe higher infection rates or adverse events among patients receiving prednisolone, which is likely explained by the small sample size and limited follow-up in our study. In contrast, vaccination status appeared relevant: four out of six herpes zoster events occurred in patients without prior herpes zoster vaccination. A recent French multicenter study similarly reported a substantial reduction in herpes zoster incidence among patients receiving antiviral prophylaxis, however prophylaxis was not used as standard in our clinic.[25]

Based on our experience and current literature, we strongly support recombinant zoster vaccination prior to treatment and consideration of antiviral prophylaxis in high-risk patients.

Beyond infections, we did not observe other notable safety concerns. Two patients experienced ischemic strokes, but given their vascular risk profiles, a direct drug causation is unlikely. Our overall impression is that anifrolumab is well tolerated in real-world use, with an infection profile similar to that of other SLE biologics, such as belimumab.

Key strengths of this study include the real-world setting and comprehensive data capture from an entire tertiary center's experience since the introduction of anifrolumab. Our group of patients likely reflects the patient phenotypes most often considered for Anifrolumab, and those with difficult-to-control SLE, making the findings relevant to everyday clinical decision-making. We used validated treat-to-target endpoints (LLDAS and DORIS), enabling meaningful comparison with other studies and highlighting the high efficacy achievable. The study also underscores important safety and management issues (like the need for zoster vaccination/prophylaxis) that trials could not fully address. However, we acknowledge several limitations, including a small sample size (36 patients), a single-center design, retrospective data collection, reliance on EMR documentation, limited follow-up for some patients, and inherent selection bias toward refractory disease.

We did not systematically assess patient-reported outcomes or health-related quality of life, as these measures are not routinely captured during standard clinic visits. However, in the PETUNIA study, anifrolumab was associated with meaningful improvements in SLE-related symptoms and multiple domains of daily functioning.[22] Future prospective studies should evaluate the impact of anifrolumab on fatigue, pain, and other patient-centered outcomes. Finally, the absence of a control group prevents definitive causal attribution, although the magnitude and consistency of response strongly support an actual treatment effect.

Conclusion

Our study provides valuable real-world evidence supporting anifrolumab's role as an effective, fast, and steroid-sparing option in difficult SLE, while also identifying practical steps to enhance its safe use. Higher rates of LLDAS and remission observed in clinical practice, compared with randomized trials, likely reflect phenotype-driven patient selection, highlighting the importance of identifying patients most likely to benefit when translating trial evidence into clinical practice.

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LN: Conceptualization, data curation, formal analysis, methodology, writing-original draft, writing-review and editing, final approval; MLL: Conceptualization, formal analysis, methodology, writing-original draft, writing-review and editing, supervision, final approval; BD: Conceptualization, writing-review and editing, final approval; MFH: Conceptualization, writing-review and editing, final approval; AT: Conceptualization, formal analysis, methodology, writing-original draft, writing-review and editing, supervision, final approval.

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Supplemental material

Supplemental material for this article is available online.

References

1. Fava A and Petri M. Systemic lupus erythematosus: diagnosis and clinical management. *J Autoimmun* 2019; 96: 1–13. https://doi.org/10.1016/j.jaut.2018.11.001
2. Hermansen ML, Lindhardsen J, Torp-Pedersen C, et al. Incidence of systemic lupus erythematosus and lupus nephritis in Denmark: a nationwide cohort study. *J Rheumatol* 2016; 43(7): 1335–1339. https://doi.org/10.3899/jrheum.151221
3. Wallace DJ. *Systemic lupus erythematosus in adults: clinical manifestations and diagnosis*. Uptodate, 2025.
4. Moysidou GS and Fanouriakis A. EULAR 2023 recommendations for the management of systemic lupus erythematosus: one step forward. *Mediterr J Rheumatol* 2024; 35(1): 63–65. https://doi.org/10.31138/mjr.130124.erm
5. Franklyn K, Lau CS, Navarra SV, et al. Definition and initial validation of a lupus low disease activity state (LLDAS). *Ann Rheum Dis* 2016; 75(9): 1615–1621. https://doi.org/10.1136/annrheumdis-2015-207726
6. van Vollenhoven R, Voskuyl A, Bertsias G, et al. A framework for remission in SLE: consensus findings from a large international task force on definitions of remission in SLE (DORIS). *Ann Rheum Dis* 2017; 76(3): 554–561. https://doi.org/10.1136/annrheumdis-2016-209519
7. Morand EF, van Vollenhoven R, Furie RA, et al. LLDAS and remission attainment with anifrolumab treatment in patients with systemic lupus erythematosus: results from the TULIP and long-term extension randomised controlled trials. *Ann Rheum Dis* 2025; 84(5): 777–788. https://doi.org/10.1016/j.ard.2025.01.016
8. Agency EM. Saphnelo (anifrolumab). Available from: https://www.ema.europa.eu/en/documents/overview/saphnelo-epar-medicine-overview_en.pdf 2022.
9. Tanaka Y and Tummala R. Anifrolumab, a monoclonal antibody to the type I interferon receptor subunit 1, for the treatment of systemic lupus erythematosus: an overview from clinical trials. *Mod Rheumatol* 2021; 31(1): 1–12. https://doi.org/10.1080/14397595.2020.1812201
10. Morand EF, Furie R, Tanaka Y, et al. Trial of anifrolumab in active systemic lupus erythematosus. *N Engl J Med* 2020; 382(3): 211–221. https://doi.org/10.1056/NEJMoa1912196
11. Morand EF, Abreu G, Furie RA, et al. Lupus low disease activity state attainment in the phase 3 TULIP trials of anifrolumab in active systemic lupus erythematosus. *Ann Rheum Dis* 2023; 82(5): 639–645. https://doi.org/10.1136/ard-2022-222748
12. Furie R, Khamashta M, Merrill JT, et al. Anifrolumab, an Anti-Interferon-α receptor monoclonal antibody, in moderate-to-severe systemic lupus erythematosus. *Arthritis Rheumatol* 2017; 69(2): 376–386. https://doi.org/10.1002/art.39962
13. Furie RA, Morand EF, Bruce IN, et al. Type I interferon inhibitor anifrolumab in active systemic lupus erythematosus (TULIP-1): a randomised, controlled, phase 3 trial. *Lancet Rheumatol* 2019; 1(4): e208–e219. https://doi.org/10.1016/S2665-9913(19)30076-1
14. Tummala R, Abreu G, Pineda L, et al. Safety profile of anifrolumab in patients with active SLE: an integrated analysis of phase II and III trials. *Lupus Sci Med* 2021; 8(1): e000464. https://doi.org/10.1136/lupus-2020-000464
15. Classen P, Boedecker-Lips S, Tomalla V, et al. Anifrolumab in systemic lupus erythematosus: real-world experience from a single academic tertiary care centre. *Clin Exp Rheumatol* 2025.
16. Tani C, Cardelli C, Zen M, et al. Anifrolumab in refractory systemic lupus erythematosus: a real-world, multicenter study. *J Rheumatol* 2024; 51(11): 1096–1101. https://doi.org/10.3899/jrheum.2024-0053

17. Sato R, Shimizu M, Kondo Y, et al. Real-world effectiveness of belimumab and anifrolumab in systemic lupus erythematosus: comparable trends in disease activity and glucocorticoid reduction. *Immunol Med* 2025; 48(4): 371–380. https://doi.org/10.1080/25785826.2025.2528296
18. Miyazaki Y, Funada M, Nakayamada S, et al. Safety and efficacy of anifrolumab therapy in systemic lupus erythematosus in real-world clinical practice: LOOPS registry. *Rheumatology* 2024; 63(9): 2345–2354. https://doi.org/10.1093/rheumatology/kead568
19. Larsen ML, Skouboe MK, Mogensen TH, et al. Dangers of herpesvirus infection in SLE patients under anifrolumab treatment: case reports and clinical implications. *Am J Case Rep* 2024; 25: e944505. https://doi.org/10.12659/AJCR.944505
20. Frodlund M, Jönsen A, Remkus L, et al. Glucocorticoid treatment in SLE is associated with infections, comorbidities and mortality-a national cohort study. *Rheumatology* 2024; 63(4): 1104–1112. https://doi.org/10.1093/rheumatology/kead348
21. Bruce IN, van Vollenhoven RF, Morand EF, et al. Sustained glucocorticoid tapering in the phase 3 trials of anifrolumab: a post hoc analysis of the TULIP-1 and TULIP-2 trials. *Rheumatology* 2023; 62(4): 1526–1534. https://doi.org/10.1093/rheumatology/keac491
22. Troldborg A, Remkus L, Eek D, et al. Anifrolumab treatment improves patient-reported quality of life and decreases disease activity and corticosteroid use in patients with systemic lupus erythematosus: a qualitative study in Denmark. *Lupus* 2024; 33(9): 962–973. https://doi.org/10.1177/09612033241261746
23. Mahmoud YW. Efficacy and safety of anifrolumab across organ domains of systemic lupus erythematosus: a systematic review and meta-analysis. *Rheumatology & Autoimmunity* 2025; 5(4): 70014.
24. Curran D, Doherty TM, Lecrenier N, et al. Healthy ageing: herpes zoster infection and the role of zoster vaccination. *npj Vaccines* 2023; 8(1): 184. https://doi.org/10.1038/s41541-023-00757-0
25. Trefond L, Chasset F, Jachiet M, et al. Efficacy of valaciclovir in preventing Herpes zoster in patients receiving anifrolumab. *RMD Open* 2025; 11(1): e005076. https://doi.org/10.1136/rmdopen-2024-005076