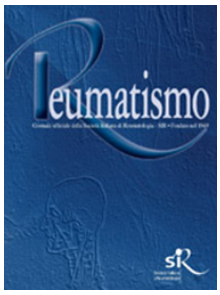

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The role of anifrolumab in reshaping the treatment landscape of extra-renal systemic lupus erythematosus

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Summary
Objective. Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder that typically requires management with immunosuppressive and anti-inflammatory treatments. The 2023 guidelines of the European Alliance of Associations for Rheumatology now recommend lowering maintenance glucocorticoid doses to ≤5 mg/day to reduce long-term health risks, a decrease from the previous 7.5 mg/day threshold set in 2019. To help achieve these reduced doses, early initiation of biologic therapies is suggested, even before conventional immunosuppressants. Belimumab and anifrolumab, the biologics currently approved for SLE treatment, have shown greater efficacy than placebo in clinical trials and similar safety profiles, supporting their use in achieving remission and enabling glucocorticoid tapering or discontinuation. This review evaluates the role of biologics, especially anifrolumab, in treating extra-renal SLE in Italy, using clinical scenarios to illustrate situations where early anifrolumab therapy could be beneficial.
Methods. Hypothetical scenarios derived from clinical practice were examined to identify real-life contexts suitable for the early initiation of anifrolumab treatment.
Results. Anifrolumab represents an effective therapeutic option for various extra-renal SLE patients. These include those who have failed to achieve or maintain remission with standard care, have contraindications to conventional immunosuppressants, are glucocorticoid-dependent, or experience mucocutaneous and musculoskeletal manifestations. Anifrolumab also offers potential benefits for patients planning pregnancy by promoting remission or low disease activity.
Conclusions. Despite its recent approval and limited real-world evidence, anifrolumab has emerged as a promising therapeutic option for non-renal lupus. We hope this review will encourage further studies on the efficacy and safety of anifrolumab in real-life SLE patient cohorts.

Introduction

Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder characterized by great heterogeneity in terms of clinical manifestations (1). Its etiology remains elusive, yet it involves a complex interplay of genetic predisposition, epigenetic modifications, and environmental triggers, resulting in aberrant immune responses (2).

The goal of SLE therapy is to control disease activity in order to prevent chronic damage development and progression, as stated in the treat-to-target recommendations (3-5). Indeed, a link between disease activity and damage has been clearly demonstrated, with deeper control of disease activity correlating with lower damage accrual (6-8). Therefore, achieving and maintaining remission is the cornerstone of current SLE management, as it is essential not only to reduce organ damage and improve survival but also to lead to improved quality of life and likely lower health-related costs (5, 9, 10). In addition, the role exerted by glucocorticoids as the main players in determining damage has been widely demonstrated and confirmed, as they pose risks of cumulative dose toxicity (11), including cataracts, cardiovascular events, osteoporosis, and fractures (12).

Finally, it should be considered that damage prevention also goes through early disease diagnosis, which follows an early introduction of the most appropriate treatment for the individual patient (13).

These aspects have been clearly addressed in the recent recommendations of the European Alliance of Associations for Rheumatology (EULAR) (5), which have introduced relevant novelties in managing SLE patients. First, these new recommendations suggest reducing the maintenance glucocorticoid dose to ≤5 mg/day (prednisone equivalent) (5), contrasting with the previous threshold of 7.5 mg/day indicated in the 2019 recommendations (14), to minimize long-term risks, with the ultimate goal of glucocorticoid withdrawal.

Biological therapies, such as belimumab and anifrolumab, targeting different immune players implicated in SLE pathogenesis (15), represent a valuable tool in the SLE treatment landscape to achieve the goal of remission, preferably without the need for glucocorticoids. Both drugs gained approval through randomized controlled trials involving comparable extra-renal SLE populations (16-21). The updated EULAR recommendations introduce the concept of early initiation of biological treatments to prevent flares, reduce glucocorticoid usage, and minimize organ damage, even without mandating the prior use of conventional immunosuppressive drugs (5).

Belimumab, an anti-B-cell stimulator human monoclonal antibody, has shown efficacy in serologically active moderate-to-severe lupus and was approved in 2011 (16, 17, 22). Numerous clinical trials and real-world studies have reported a significant glucocorticoid-sparing effect of belimumab in SLE management (23-30).

Anifrolumab, a fully human IgG1k monoclonal antibody targeting interferon (IFN)-α/β receptor (11), was approved in 2021 (17, 18). It has demonstrated efficacy in treating extra-renal SLE, controlling disease activity, reducing flares, and facilitating glucocorticoid dose reduction and discontinuation (18-21).

In Italy, both belimumab and anifrolumab are fully reimbursed by the National Health Service under class H, meaning they are available at no cost to patients but are restricted to hospital use (31, 32). Both drugs are indicated as adjunctive therapy in adult patients with active, autoantibody-positive SLE. Belimumab is specifically recommended for patients with high disease activity (*e.g.*, anti-dsDNA positivity and low complement levels) despite standard therapy, whereas anifrolumab is indicated for moderate to severe forms of the disease that persist despite standard treatment (31, 32). While we found it challenging to retrieve the specific reimbursement criteria throughout other European nations, the indications generally reflect those from the European Medicines Agency (33, 34). The mechanism of reimbursement, however, distinguishes Italy from other countries, including the USA, where the Food and Drug Administration has issued similar indications for anifrolumab

and broader indications for belimumab (for all patients with SLE aged more than 5 years, without specifying the degree of disease activity) (35, 36). However, the reimbursement system in the USA is predominantly structured around private insurance providers, leading to significant variability in drug coverage and patient out-of-pocket expenses (37). This approach can, at times, restrict or delay access to novel therapies, particularly for individuals with inadequate insurance coverage or those unable to afford high out-of-pocket costs (37). This also distinguishes Italy from China, where reimbursement policies may vary or impose financial burdens on patients (38). The national reimbursement criteria set by the Italian Medicines Agency facilitate broad access to biologics in clinical practice, allowing physicians to focus primarily on optimizing their therapeutic use rather than navigating administrative or financial constraints.
This review aims to offer an expert opinion on the use of biological drugs in the Italian therapeutic landscape for extra-renal SLE, particularly focusing on the role of the newly licensed drug, anifrolumab, in the therapeutic paradigm of SLE.

Methods

The authors conducted a comprehensive, non-systematic review of current literature to assess the role of biologics, particularly anifrolumab, in treating SLE. This review examined hypothetical clinical scenarios based on the authors' real-life clinical practice and available scientific data from randomized controlled trials and expert opinion on patient management under real-world conditions. The focus was to identify clinical contexts where early initiation of anifrolumab might benefit patients with extra-renal SLE.

Expert opinion: clinical scenarios for biological treatment in systemic lupus erythematosus patients

Although anifrolumab has been approved for adult patients with moderate to severe SLE refractory to standard therapy, uncertainty remains regarding the selection criteria for patients eligible for earlier anifrolumab treatment in clinical practice. The forthcoming expert opinion section is based on both safety and efficacy evidence for anifrolumab across various organ manifestations in different subsets of SLE patients (18-20) and personal experience. It aims to develop hypotheses to identify patients likely to benefit from adding anifrolumab to the standard of care (SoC), particularly those with high unmet needs (Figure 1).

Moderate-to-severe systemic lupus erythematosus patients who fail to achieve or maintain remission with standard of care

Despite advancements in treatment, SoC comprising hydroxychloroquine, immunosuppressants, and corticosteroids often falls short. Only a minority of patients achieve complete remission with these treatments, and many experience disease flares, leading to increased organ damage and mortality (39-41). This further emphasizes the need for alternative therapies when first-line conventional treatments fail. Biologics, such as anifrolumab and belimumab, offer new hope in this context. The available data have shown that they not only help achieve but also sustain remission, which is crucial for minimizing long-term steroid use (21, 23, 42-44). Anifrolumab has demonstrated efficacy in rapidly reducing symptoms and steroid doses to below 5 mg/day, with many patients being able to discontinue steroids completely (21, 44). Similarly, belimumab has shown its ability to maintain disease control, thus facilitating steroid tapering and potentially supporting steroid-free management in SLE (45, 46).
In patients with moderate or severe disease who fail to achieve remission despite treatment with hydroxychloroquine, immunosuppressants, and corticosteroids, anifrolumab offers a potential solution to achieve this goal (44). Furthermore, if the patient experiences flares preventing the

maintenance of remission over time, adding biologics to the treatment regimen may be indicated to regain and sustain remission (44, 47).
Intriguingly, preliminary data suggest that earlier remission achievement is associated with less damage accrual (48), a higher probability of steroid discontinuation in the longer term (49), and that the use of biologics early in the disease course is associated with a higher response (23).
The role of biologics in contributing to achieving remission and reducing steroid dependence (21, 25, 28-30, 50) highlights their utility early in the disease course to improve long-term outcomes.

Adverse effects/contraindications of conventional immunosuppressants
SLE is characterized by various courses, including relapsing-remitting and persistently active patterns (51). The complexity of managing SLE extends beyond disease activity fluctuations and encompasses the burden of comorbidities. Distinguishing between disease-related and treatment-related morbidity poses challenges; nevertheless, evidence suggests that patients with SLE exhibit an increased prevalence of hypertension, dyslipidemia, obesity, diabetes, cardiovascular and cerebrovascular diseases, infectious complications, osteoporosis, and malignancies (52). This intricate interplay between disease activity and comorbidities necessitates a tailored approach to therapy, where the efficacy and safety profiles of medications must be carefully weighed against the backdrop of multiple disease-specific and patient-specific factors. As indicated by recent EULAR recommendations, conventional and biological immunomodulatory/immunosuppressive agents are the primary options to consider in controlling disease activity, reducing flares, and facilitating glucocorticoid dose reduction (5). However, conventional immunosuppressants may pose challenges in management, as cytopenias, kidney injury, and hepatic dysfunction are potential adverse events associated with some of these drugs, such as azathioprine and methotrexate (53, 54). In addition, contextualizing these alterations in clinical practice can be intricate, as they might be caused by the therapy itself or the underlying active lupus disease.
In light of this, for SLE patients with comorbidities or contraindications to conventional immunosuppressants, in the presence of non-renal active disease despite hydroxychloroquine and glucocorticoid therapy, early treatment with biological immunosuppressants, such as belimumab or anifrolumab in combination with SoC, may be a preferable option. This approach not only offers potential benefits in terms of efficacy compared with SoC alone but also underscores considerations regarding the improved safety profile (21, 55).

Glucocorticoid-dependent hematological manifestations of systemic lupus erythematosus
Hematological abnormalities are frequently encountered in SLE, both at the time of diagnosis and throughout the course of the disease. The most common hematological manifestations include hemolytic anemia (10% of patients), leukopenia (50-60%), and thrombocytopenia (10-40%), with different severity levels (56, 57). The high frequency of SLE-related hematological manifestations has led to their inclusion in SLE classification criteria (58). From a pathogenic point of view, various mechanisms have been suggested, including reduction in bone marrow production, spleen sequestration, and peripheral destruction mediated by autoantibodies (57). Regarding treatment, the most recent EULAR recommendations (5), referring only to severe autoimmune thrombocytopenia, suggest using high doses of glucocorticoids, with or without intravenous immunoglobulin G and/or rituximab and/or high-dosage cyclophosphamide. Moreover, for the maintenance phase, rituximab, azathioprine, mycophenolate, or cyclosporine should be considered (14).
However, in real-life contexts, we must manage not only SLE patients with acute thrombocytopenia but also those in whom immunosuppressive drugs are unable to control this manifestation without the aid of glucocorticoids in the long term. A subgroup of SLE patients with recurrent episodes of thrombocytopenia, initially treated with glucocorticoids combined with intravenous

immunoglobulins, conventional immunosuppressive drugs, or rituximab, may experience transient improvements. In our experience, many patients treated with these combinations fail to reduce glucocorticoid dose below 5 mg/day in the long term because of thrombocytopenia recurrences, with a high risk of glucocorticoid-related organ damage. In this scenario, biological drugs, including anifrolumab, in combination with SoC, could play a role in controlling disease manifestations and in sparing glucocorticoids. However, it has to be underlined that due to the lack of trials specifically designed to evaluate the role of these drugs in SLE-related thrombocytopenia, encouraging results on biologics on this manifestation are based on post-hoc analyses (59, 60) and observational reports (61, 62). In the study by Dong *et al*. (61), belimumab treatment reduced anti-phospholipid antibodies while increasing platelet count in SLE patients with anti-phospholipid antibody-associated immune thrombocytopenia. Similarly, Nakayama *et al*. (62) reported that two patients with glucocorticoid-resistant SLE-associated immune thrombocytopenia achieved remission with belimumab. In the study by Manzi *et al*. (59), significantly fewer patients treated with belimumab experienced worsening in the BILAG hematological domain (1 mg/kg) and the SELENA–SLEDAI hematological domain (10 mg/kg) compared with placebo. Regarding anifrolumab, Casey *et al*. demonstrated that in patients with moderate-to-severe SLE, anifrolumab treatment, in addition to SoC therapy, led to a rapid and sustained reversal of SLE-associated thrombocytopenia, normalizing platelet concentrations more effectively than placebo (60).
Based on our experience, in the event of a severe platelet drop while on therapy with hydroxychloroquine and conventional immunosuppressants and/or belimumab, the use of anifrolumab can lead to stable platelet counts and effective control of other disease manifestations while sparing glucocorticoids.

Mucocutaneous manifestations of systemic lupus erythematosus
Mucocutaneous manifestations are highly prevalent in SLE patients, occurring in approximately 70% of patients and being the second most frequent clinical manifestation of the disease (63, 64).
A subgroup of patients displaying mucocutaneous SLE has subacute cutaneous lupus erythematosus (SCLE) (65). These patients can develop systemic disease symptoms in 50% of cases (*i.e*., polyarthralgia, low complement, positive anti-dsDNA) and usually have anti-SSA positivity (66). It is rather common for these patients to be refractory to the first-line treatment based on glucocorticoids (*i.e*., prednisone 25 mg/day, then tapered) and hydroxychloroquine 5 mg/kg/day; for example, the patient may experience an exacerbation of the subacute skin rash and polyarthralgia during glucocorticoid tapering. In these cases, belimumab could be added to first-line treatment before or after the failure of traditional immunosuppressants, such as methotrexate. Given the local production of IFN in the skin of patients with SLE (67-70), the recent approval of anifrolumab, a new anti-IFN drug (71), paves the way for the use of new molecules, not only in refractory cases but also after the first-line treatment. The mechanism of action of anifrolumab suggests that, in refractory patients, transitioning from belimumab or traditional immunosuppressants to anifrolumab can lead to rapid, complete resolution of SCLE after a few infusions, as reported in our clinical practice experience. The TULIP-1 and TULIP-2 studies reported a ≥50% reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI)-Activity and a ≥50% reduction in tender and swollen joint count (72, 73). Skin responses were achieved early in treatment, as observed in another recent TULIP *post-hoc* analysis reporting sustained improvements in overall SLE disease activity and skin responses compared with placebo as early as week 8 after anifrolumab treatment (44). Several case studies and case series have provided evidence supporting its effectiveness for refractory mucocutaneous manifestations in SLE, reporting a quick reduction in CLASI in almost all cases within 8 weeks of treatment (74-79). These case reports align with our clinical practice experience in refractory patients, even those previously treated with belimumab,

who obtain a rapid, complete resolution of cutaneous manifestations after a few infusions of anifrolumab.

Musculoskeletal manifestations of systemic lupus erythematosus

Joint and tendon inflammation are among the most common SLE manifestations, affecting up to 90% of patients and being reported in up to 60% of disease flares (80, 81). Prolonged or recurrent joint inflammation is a major determinant of higher cumulative glucocorticoid dose, impaired quality of life, and increased risk of developing Jaccoud's deformity (82, 83). Synovitis can mimic rheumatoid arthritis, with persistent pain, swelling, stiffness, and disability, but is usually transient, leading physicians to underestimate the severity of joint involvement in SLE (84). Gabba *et al.* demonstrated that 34% of SLE patients considered to have mild musculoskeletal disease activity, scoring C on the British Isles Lupus Assessment Group (BILAG)-2004 index, showed positive power-Doppler signal on joints and/or tendons ultrasound of the hands, suggesting they should be considered to have active disease, scored B on the BILAG, and deserve treatment changes (85). Later, the definition of inflammatory arthritis in the BILAG-2004 index was changed to classify patients with ultrasonographic synovitis and/or tenosynovitis as more active and more likely to respond to treatment changes (86).

For patients with arthritis or those with arthralgias and ultrasonographic synovitis and/or tenosynovitis despite hydroxychloroquine treatment with or without immunosuppressants, adding a biological drug could be a valid therapeutic approach to rapidly resolve inflammation, reduce the risk of musculoskeletal flare and glucocorticoid use over the long term.

Family planning

SLE is a chronic condition that frequently affects young women of childbearing age (87). Therefore, patients' desires regarding family planning are of fundamental importance in the management of women living with this chronic disease.

Despite improvements in recent decades, the rate of obstetrical and neonatal complications in SLE patients remains higher than in the general obstetrical population (88). It has been widely demonstrated and is recommended in the current guidelines (89-92) to explain to patients the importance of planning a pregnancy when SLE is either in remission or a state of low disease activity, as active disease could increase the rate of pregnancy complications (93). A careful evaluation of treatment strategies is necessary for all patients who want to conceive because rapid and sustained disease remission must be obtained using treatments that are compatible with preconception, pregnancy, and breastfeeding. In fact, several immunosuppressant drugs must be stopped months before conception (*i.e.*, mycophenolate mofetil, methotrexate) because of teratogenic risks (94), and corticosteroids should be used at the lowest possible dosage because of the increased risk of several pregnancy-related complications, such as gestational diabetes, hypertensive disorders of pregnancy, and preterm delivery (95, 96). Despite some immunosuppressants being considered safe during pregnancy, such as azathioprine (97), calcineurin inhibitors (98), tacrolimus (99), and cyclosporine (100), only a minority of patients achieve remission with them (101). In this context, biological agents could be a possible option for patients wishing to conceive because their use, at least preconceptionally, could increase the chance of achieving remission or low disease activity and reduce the need for corticosteroids. However, the use of biological treatments during pregnancy remains debated: current guidelines may allow the use of belimumab in early pregnancy or even later if no other pregnancy-compatible drugs are suitable (92), whereas no sufficient data are available on anifrolumab.

Discussion

Reshaping the treatment landscape: evidence on the role of biologics in achieving remission or low disease activity

Despite substantial progress in understanding the pathophysiology of SLE and the advent of new treatments that have enhanced survival rates, SLE patients remain vulnerable to ongoing organ damage (102, 103) due to disease activity and glucocorticoid intake. Furthermore, a significant proportion of patients are either unresponsive to conventional therapies or experience drug-induced toxicity (104-107). Additionally, SLE patients also continue to experience a diminished health-related quality of life despite positive outcomes in clinical and laboratory measures and a notably higher mortality rate (108, 109).

Belimumab and anifrolumab, the biological drugs approved for SLE treatment, serve as valuable tools for managing SLE and facilitating the reduction and discontinuation of glucocorticoid therapy (21, 25, 28-30, 47, 50), as highlighted by the updated EULAR recommendations (5), which refrain from establishing a hierarchy between belimumab and anifrolumab because of their distinct mechanisms of action and the absence of direct comparative trials.

Anifrolumab has been recently approved for the treatment of moderate-to-severe SLE (71, 110). The results obtained in the clinical trials (20, 21, 47, 111) and the limited real-world evidence available to date are highly encouraging, both in terms of efficacy and safety (50).

Post-hoc analyses of the phase IIb MUSE and phase III TULIP-1 and TULIP-2 trials revealed a significantly higher proportion of patients achieving lupus low disease activity state (LLDAS) when treated with anifrolumab compared with the placebo arm (both plus SoC) by week 52 (47, 111). In particular, the combination of anifrolumab with SoC demonstrated efficacy in achieving LLDAS compared with SoC alone in patients with moderate to severe disease during the 3-year TULIP-LTE period (42); in addition, anifrolumab was linked to earlier attainment of LLDAS, longer cumulative time spent in LLDAS, and a greater chance of sustained LLDAS than placebo (47). These data align with our clinical experience, where anifrolumab in combination with SoC helps achieve remission or LLDAS after the failure of SoC, also when combined with belimumab.

Furthermore, *post-hoc* analyses showed a notably higher number of patients achieving DORIS remission by week 32, suggesting an earlier achievement of remission with anifrolumab treatment compared with placebo (47).

Further analysis of TULIP-1 and TULIP-2 demonstrated the efficacy of anifrolumab after 52 weeks of treatment in patients with both established and recent-onset disease (112). Moreover, anifrolumab in combination with SoC exhibited a notable increase in the mean improvement in the SLEDAI-2K during the phase III LTE trial compared with SoC alone (21). Positive treatment differences favoring anifrolumab versus placebo were observed across subgroups based on baseline standard therapies, even in those patients not taking immunosuppressants (113). Anifrolumab showed greater improvements versus placebo in the musculoskeletal, mucocutaneous, and immunological systems at week 52 in *post-hoc* analyses of pooled data from the TULIP-1 and TULIP-2 trials (18, 20, 72, 73).

The control of skin and musculoskeletal manifestations is pivotal to the successful management of SLE, as studies on patients with long-standing SLE indicate that those with skin and joint involvement have a reduced likelihood of achieving LLDAS or remission (114, 115). The efficacy in mucocutaneous manifestations is likely due to anifrolumab-dependent downregulation of type I IFN production in the skin (69, 70). In SLE patients, keratinocyte apoptosis leads to the release of nucleic acids and damage-associated molecular patterns (70) that accumulate due to impaired phagocytic clearance (116), activating pattern recognition receptors on keratinocytes and increasing IFN-regulated gene production (117). Elevated type I IFN levels may prime plasmacytoid dendritic cells, creating a proinflammatory environment (70, 118) and inducing granzyme B-expressing

CD8+ T cells (119, 120) and autoantibody production by B cells (121). By inhibiting IFNAR1, anifrolumab blocks this cascade, explaining its rapid efficacy in mucocutaneous manifestations (44).
Furthermore, encouraging results are emerging regarding the efficacy of anifrolumab in controlling SLE-related hematological manifestations, as seen in our clinical experience, particularly with refractory thrombocytopenia.
The evaluation of complete blood counts of lymphocytes, neutrophils, platelets, and monocytes in patients enrolled in the MUSE phase IIb trial reported a rapid and sustained reversal of SLE-associated lymphopenia, neutropenia, monocytopenia, and thrombocytopenia with anifrolumab in addition to SoC compared with placebo, independent from glucocorticoid tapering (60). The pathogenic link between these manifestations and the IFN pathway has not been fully clarified (60). However, a possible suppressive effect of IFN on the bone marrow has been previously described, suggesting that high IFN expression could result in anemia, neutropenia, lymphopenia, and thrombocytopenia (122).
The achievement of LLDAS or, even better, remission is a fundamental prerequisite for women with SLE who are planning a pregnancy (104, 123), as outlined earlier. A recent real-world study in Asian patients who received anifrolumab for the failure of SoC and patients who experienced lupus flares despite treatment reported LLDAS and DORIS remission being achieved in 66% and 22% of patients, respectively, after 26 weeks of treatment, without the need to increase the glucocorticoid dose (50). The precocious attainment of LLDAS and the higher chances of remission associated with anifrolumab treatment compared with the SoC make it a valuable therapeutic option to be used during the preconception period for women with SLE.

Optimizing glucocorticoid tapering with biological agents
Adjusting the remission glucocorticoid threshold to less than 5.0 mg/day of prednisone equivalent provided better protection against mortality than remission (124), and the mortality risk positively correlates with the glucocorticoid dose (125). Nonetheless, long-term glucocorticoid treatment ≤5 mg/day of prednisone equivalent is still associated with damage accrual (44, 126).
Therefore, achieving glucocorticoid-free remission offers the highest level of protection against damage (124). However, glucocorticoid discontinuation remains a challenging goal, as evidenced by real-world studies reporting that only less than 10-15% of patients are able to withdraw glucocorticoids (127-129).
Our clinical experience suggests that anifrolumab serves as a valuable tool for reducing the reliance on glucocorticoids in SLE management, as it allows for good disease control and a low occurrence of severe flares even after glucocorticoid discontinuation. This aligns with the results obtained during the clinical development phase of anifrolumab (18, 20), which demonstrated greater glucocorticoid dose reductions than placebo, even in the long term (21) and in active lupus nephritis (130). In particular, *post-hoc* analysis of TULIP trials revealed that 50.5% of anifrolumab patients on prednisone ≥10 mg/day achieved sustained tapering versus 31.8% for placebo (131). A recent real-world study by Miyazaki *et al.* supported the results of clinical trials, finding reduced disease activity and fewer glucocorticoid escalations in SLE patients treated with anifrolumab compared with the SoC group (50). Additionally, patients receiving anifrolumab plus SoC showed greater glucocorticoid dose reductions and longer durations at ≤7.5 mg/day by week 52 compared to those receiving placebo plus SoC (44). This provides valuable support to clinicians in initiating glucocorticoid withdrawal.
Given its ability to facilitate glucocorticoid tapering while maintaining disease control and its favorable safety profile (11, 21), early initiation of anifrolumab treatment, particularly in patients

with high-risk features, could potentially improve disease outcomes and reduce morbidity and mortality (14, 21, 44, 131).

Conclusions

Accumulating evidence supports the role of biologics in controlling disease activity and promoting remission, allowing for a reduction in glucocorticoid dosage and associated damage. Although the approval of anifrolumab is recent, and therefore, scarce evidence is available from clinical practice, the data obtained so far are highly encouraging. It should be emphasized that the expert opinion section delineates “real-life” clinical practice in Italy, which is influenced by the prescription eligibility criteria and reimbursement policies for biological drugs in treating SLE in this country. Despite promising outcomes, we acknowledge that limited real-world evidence is available on the use of anifrolumab, owing to its recent regulatory approval (71, 110). Given the high potential of anifrolumab, we hope the present review will prompt further studies on the efficacy and safety of anifrolumab in real-life cohorts of SLE patients.

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Figure 1. Summary of the areas where anifrolumab may address the unmet needs of systemic lupus erythematosus patients, based on the expert opinions of the authors.