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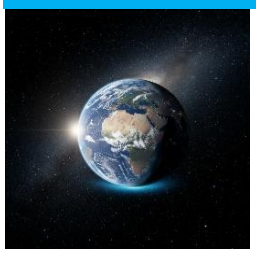

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Anifrolumab in the Treatment of Lupus Nephritis (LN): From Mechanism of Action to Clinical Perspectives

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Abstract

Background: Lupus nephritis (LN) is one of the most severe and prognostically unfavourable organ complications of systemic lupus erythematosus, which significantly affects patient morbidity and mortality. Despite advances in immunosuppressive therapy, some patients do not achieve sustained renal remission, indicating a need for targeted treatment. Increasing evidence points to the important role of type I interferon signalling in the pathogenesis of SLE and LN.
Aim: This review analyses current data on the mechanism of action, clinical efficacy and safety profile of anifrolumab and evaluates its potential role in the treatment of lupus nephritis.
Materials and Methods: A narrative literature review was conducted using PubMed and Embase databases, including randomized clinical trials, extended studies and international treatment guidelines published up to 2024. Particular attention was paid to the phase II TULIP-LN trial and key studies assessing anifrolumab in systemic lupus erythematosus.
Results: Anifrolumab demonstrated a beneficial effect on immune activity and extra- renal manifestations of SLE. In patients with active lupus nephritis, intensified dosing regimens were associated with a higher rate of complete renal response, greater reduction in proteinuria, improvement in estimated glomerular filtration rate, and more effective glucocorticoid tapering compared with placebo. Although the primary endpoint of the TULIP-LN study was not met, secondary and exploratory results suggest potential renal benefits, particularly with intensified dosing. The safety profile was acceptable, with infections, particularly herpes zoster, being the most frequently reported adverse events.

Conclusions: Anifrolumab represents a promising targeted treatment for lupus nephritis. Phase II data indicate potential clinical benefits, but its definitive place in therapy requires confirmation in ongoing phase III trials.

Keywords: lupus nephritis; systemic lupus erythematosus; anifrolumab; type I interferon; biological therapy; targeted treatment

I. Introduction

1.1 Lupus nephritis: a clinical challenge

Lupus nephritis is an inflammatory disorder arising from the deposition of immune complexes and other components of the immunologic response within renal tissue [1]. It represents one of the most frequent and clinically severe complications of systemic lupus erythematosus [2]. Thirty-five percent of SLE patients in the United States have clinical evidence of nephritis at the time of diagnosis, and 50%-60% will develop nephritis within the first 10 years of the disease [1].

The pathogenesis of LN is closely related to the production of autoantibodies (especially anti-dsDNA) that form immune complexes. The deposition of these complexes in the glomeruli leads to the activation of the complement system and the initiation of an inflammatory process that causes damage to renal structures. In the intrarenal pathogenesis of lupus nephritis, a key mechanism is the direct binding of antibodies to various autoantigens within the kidney, rather than solely the deposition of circulating immune complexes. Clinically, this process manifests as proteinuria, haematuria and progressive deterioration of the glomerular filtration function of the kidneys [3].

LN develops in approximately 40-60% of adult patients with SLE and significantly worsens their prognosis. It is a major determinant of mortality and the risk of permanent organ damage in patients with SLE [2]

Classification of lupus nephritis according to ISN/RPS 2018

The basis for the histopathological assessment of LN is the revised version of the classification of lupus nephritis published in 2018 and developed by the International Society of Nephrology and Renal Pathology Society (ISN/RPS). The criteria for individual classes have been clarified and the assessment of activity and chronicity of changes has been standardised [4]. Below is a summary of the classification of LN [4].

Table 1. Classification of lupus nephritis according to ISN/RPS 2018

Class	Histopathological characteristics	Clinical significance
I	Minimal mesangial changes; deposits in the mesangium; no changes in light microscopy	Most often asymptomatic; mild course
II	Mesangial proliferation with mesangial deposits	Low-grade proteinuria, with overall favourable prognosis
III	Focal proliferative lesions affecting fewer than 50 percent of glomeruli, with active and/or chronic components; crescents may be present	Requires intensive immunosuppressive therapy
IV	Diffuse proliferative lesions involving at least 50 percent of glomeruli; segmental or global in distribution, with crescents frequently observed	The most severe and most common form of lupus nephritis
V	Membranous pattern of injury	Nephrotic syndrome is frequently present
VI	At least 90 percent of glomeruli demonstrating global sclerosis	Management is primarily renoprotective, with no demonstrable benefit from intensive immunosuppression

The choice of therapy for lupus nephritis is determined by the histopathological class, the degree of inflammatory activity, and the severity of the clinical presentation. According to current KDIGO (2021) and EULAR (2019/2023) guidelines, classes III and IV require intensive induction therapy, whereas class V is managed based on the degree of proteinuria and the presence or absence of concomitant proliferative lesions [5-7].

Induction therapy

1. Mycophenolate mofetil (MMF)

Mycophenolate mofetil is currently one of the first-line drugs for inducing remission in class III and IV in patients with SLE. Compared to cyclophosphamide, the efficacy of MMF is comparable or better with a more favourable safety profile. The standard dose of MMF is 2-3 g/day. Due to the gonadotoxicity of cyclophosphamide, MMF is the preferred drug in women of childbearing age [5,7].

2. Cyclophosphamide (CYC)

Cyclophosphamide is an alternative first-line induction agent to MMF for patients with active class III/IV lupus nephritis. Both MMF and low-dose intravenous cyclophosphamide are

recommended options in KDIGO 2021. The monthly regimen using 0.5–1 g/m² for 6 months is among the accepted dosing schemes [5].

3. Glucocorticosteroids (GCS)

Glucocorticosteroids remain the mainstay of induction therapy in LN. Currently, high intravenous glucocorticoid pulses for a short period followed by rapid tapering of oral doses are preferred. This is to minimise the risk of metabolic, cardiovascular and infectious complications [7].

Maintenance treatment

Once remission has been achieved, treatment enters the maintenance phase, which should be continued for at least 3 years. The standard first choice is MMF (1-2 g/day) or azathioprine in women who are planning pregnancy or who cannot tolerate MMF therapy [5,7].

The use of appropriate maintenance therapy is crucial in preventing relapses, which occur at a high rate in patients with LN.

Belimumab in LN therapy

Belimumab, a human monoclonal antibody against BLyS, is the first biologic drug formally registered for the treatment of LN. Referring to the BLISS-LN study, the addition of belimumab to MMF or CYC was shown to increase the rate of renal remission and reduce the frequency of relapses [8]. Currently, according to EULAR 2023, it is recommended to consider adding belimumab as an add-on treatment in classes III, IV and selected patients with class V disease accompanied by significant proteinuria [7].

Limitations of current treatment methods

Despite the use of immunosuppression with proven efficacy in the treatment of lupus nephritis, a significant proportion of patients do not achieve complete renal remission, and some will experience progressive loss of renal function [5,7]. The current limitations of existing therapies include:

- insufficient efficacy in some patients with LN, especially in proliferative classes;
- complications of therapy, especially when using GCS and CYC;
- delayed clinical responses;
- lack of treatment directly targeting the interferon axis, which is important in the pathogenesis of SLE and LN;
- high risk of progression to chronic kidney disease despite the use of standard treatment regimens.

The above limitations demonstrate the need to develop more selective targeted therapies that would improve treatment efficacy and reduce the risk of adverse effects.

1.2 The pathogenesis of SLE and the role of type I interferons

Excessive activation of the type I interferon axis plays a key role in the pathogenesis of systemic lupus erythematosus. The serum of SLE patients contains circulating immune complexes containing autoantibodies and DNA, capable of activating plasmacytoid dendritic cells that produce large amounts of IFN-α [9]. Type I interferons promote the maturation of antigen-presenting cells, stimulate the differentiation of B lymphocytes into plasma cells producing autoantibodies (including anti-dsDNA) and enhance T lymphocyte activation. Chronic excessive activation of the IFN-I pathway causes chronic autoimmunity and promotes organ damage, including lupus nephritis[9]. The role of the IFN-I pathway in patients with SLE justifies the development of IFNAR1 receptor-blocking therapies, such as anifrolumab.

II. Anifrolumab, an anti-interferon drug.

2.1 Anifrolumab- characteristics of the molecule.

Anifrolumab is a human IgG1κ monoclonal antibody that binds to the IFNAR1 subunit of the type I interferon receptor. Inhibition of this receptor suppresses activation of the JAK-STAT pathway, which leads to a reduction in type I interferon-induced genes and a decrease in SLE disease activity [10,11].

This mechanism distinguishes anifrolumab from other agents that target only IFN- α, because it blocks the receptor shared by all type I interferons [10]. In patients with active lupus nephritis, lower drug concentrations have been observed, which was associated with an increased clearance in individuals with proteinuria. This indicates the need for a more intensive dosing regimen in patients with LN and proteinuria [12].

Anifrolumab is approved for the treatment of moderate to severe SLE, while its efficacy in lupus nephritis is still being evaluated in clinical trials [11].

2.2 Impact of anifrolumab on the immune system.

Anifrolumab blocks the IFNAR1 subunit, thereby inhibiting signaling of all type I interferons and reducing the interferon gene signature [11]. The agent suppresses dendritic cell activation, limits antigen presentation, and attenuates excessive T-cell activation. It also interferes with the differentiation of B cells into plasma cells, potentially resulting in a reduction in autoantibody production [13, 14].

III. Clinical evidence in lupus nephritis

3.1 Clinical trials of anifrolumab in systemic lupus erythematosus.

TULIP-1 was a randomised, double-blind phase 3 clinical trial enrolling patients aged 18 to 70 years with moderate to severe SLE activity despite standard therapies. Patients with active lupus

nephritis and those with central nervous system involvement were excluded. Participants were randomly assigned to the placebo group, the 150 mg anifrolumab group or the 300 mg anifrolumab group. The drug was administered intravenously every 4 weeks for 48 weeks. Standard treatment was continued except for attempts to reduce it in patients taking oral GCS at dose of 10 mg/day or more. The primary endpoint of TULIP-1 was to demonstrate a difference between the percentage of patients receiving anifrolumab 300 mg who achieved a response according to the SRI-4 index compared to patients receiving placebo. Background therapy was continued, except for attempts to taper treatment in patients receiving oral glucocorticoids at a dose of 10 mg per day or higher. The primary endpoint was not met and secondary endpoints were not formally tested for statistical significance. Secondary endpoints evaluated differences between the anifrolumab 300 mg group and placebo with respect to:

- the proportion of patients in whom glucocorticoid dose could be tapered from at least 10 mg per day at baseline to 7.5 mg per day or less between weeks 40 and 52;
- the proportion of patients with a baseline CLASI score of at least 10 who achieved at least a 50 percent reduction in this score by week 12;
-annualized flare rate through week 52;
- the proportion of patients with a high interferon gene signature who achieved an SRI-4 response at week 52;
- the proportion of patients who achieved an SRI-4 response at week 24 [10].

Several secondary endpoints showed favorable trends. Among patients treated with anifrolumab 300 mg, a beneficial effect on glucocorticoid tapering was observed. Forty-nine percent of patients receiving glucocorticoids at a dose of 10 mg/day or more achieved dose reduction to 7.5 mg per day or less, compared with 32 percent in the placebo group. A higher proportion of patients also demonstrated at least a 50 percent improvement in cutaneous disease activity assessed by the CLASI score (baseline score at least 10) relative to placebo[10].

In the TULIP-2 study, patients were randomly assigned in a 1:1 ratio into two groups: one receiving intravenous anifrolumab at a dose of 300 mg every 4 weeks for 48 weeks, and the other receiving a placebo. In the TULIP-2 study, as in TULIP-1, patients with active lupus nephritis and patients with neuropsychiatric lupus were excluded. The primary endpoint at week 52 was response to treatment as assessed by the British Isles Lupus Assessment Group (BILAG)-based Composite Lupus Assessment (BICLA) [11].

Secondary endpoints of this study included: BICLA response in patients with a high interferon gene signature at baseline, reduction in steroid doses, reduction in skin lesion activity, reduction in joint pain and swelling and reduction in disease flares [11].

Of the 180 patients receiving anifrolumab 47.8% achieved a BICLA response, compared with 31.5% of the 182 patients receiving placebo, meeting the primary endpoint with a statistically significant difference. In patients with a high interferon gene signature in the anifrolumab group, 48% responded compared with 30.7% in the placebo group. In the group of patients with low interferon gene signature, 47.7% versus 35.5%, respectively [11].

Secondary endpoints demonstrated the efficacy of anifrolumab in reducing skin lesion activity and steroid doses. No statistically significant benefit was demonstrated for arthritis-related endpoints, and effects on disease flare rates were not conclusive [11].

3.2 Phase II Study TULIP-LN- Analysis of Key Results

TULIP-LN was double- blind phase II trial involving 147 patients. Patients were divided into a 1:1:1 ratio and received the following every 4 weeks: 300mg of anifrolumab intravenously, an intensified dosing regimen of 900mg x3 followed by 300mg of anifrolumab intravenously and placebo therapy, alongside standard therapy (oral GCS, MMF). The primary endpoint was change in baseline 24- hour urine protein- creatinine ratio (UPCR) at week 52 for patients with anifrolumab treatment vs placebo groups. The secondary endpoint was: complete renal response (CRR) at week 52. Among the exploratory endpoints, more stringent criteria for complete renal response (CRR) and sustained reduction in glucocorticoid dose to ≤7.5 mg/day at weeks 24-52 were evaluated [12].

Patients receiving anifrolumab showed an improvement in UPCR of 69%, while the placebo group showed an improvement of 70%. At week 52, a higher percentage of patients treated with anifrolumab in the intensive regimen achieved a daily protein/ creatinine ratio (UPCR) of ≤0.7 mg/mg compared to both the standard-dose regimen and the placebo [12].

The secondary endpoint assessed the percentage of patients achieving complete renal response (CRR) at week 52. The results in the combined anifrolumab and placebo groups were virtually identical (31% vs 31.1%). It was observed that intensive regimen anifrolumab therapy was associated with a higher CRR than placebo (45.5% vs 31.1%). In contrast, in the standard-dose regimen, this rate was lower than in placebo group. (16.3% vs 31.1%) [12].

Exploratory outcomes consistently favored the IR regimen. The percentage of patients who maintained a reduction in oral glucocorticoid dosage to ≤7.5 mg/day was higher in the anifrolumab intensive regimen group than in the placebo group (55.6% vs 33.3%). In contrast, in the standard-dose regimen, these values were similar to placebo (35.5% vs 33.3%) [12].

To continue participating in the second year of study, patients were required to achieve at least a partial renal response and meet the criteria for glucocorticoid reduction. Of the 147 patients enrolled in TULIP-LN, 101 completed year 1 of the study and 75 of these continued into year

2. Among the 145 patients, a higher percentage of patients achieved complete renal response in the intensive-dose group (25%) at week 104 compared to the standard-dose group (18.6%) or placebo (17.8%) [15].

The improvement in estimated glomerular filtration rate was greater in both groups receiving anifrolumab compared to the placebo group. A reduction in GCS dosage from ≥20 mg/day to ≤5 mg/day during weeks 80-104 was achieved in 36.1% of patients in the high-dose group, 30.3% in the placebo group and 22.6% in the base-dose group. Concurrent achievement of complete renal response (CRR) and reduction in GCS dose was observed in 25% of patients treated with high doses, 17.8% of patients in the placebo group and 18.6 % of patients treated with standard doses. The mean daily urinary protein/ creatinine ratio (UPCR) improved from baseline to week 104 by 83% in the anifrolumab high-dose group, 80% in the standard-dose group and 80% in the placebo group [15].

In both groups receiving anifrolumab, a greater reduction in non-renal SLEDAI-2K scores was observed compared to placebo, visible as early as week 4 and persisting until week 104 of observation. Patients treated with anifrolumab also showed improvement in serological parameters, including a decrease in anti-dsDNA antibody titres and an increase in C3 concentration, with the beneficial changes being more pronounced in the high-dose regimen. In the placebo group, serological markers showed variability without a clear trend. Cumulative proteinuria throughout the 104-week observation period was consistently lower in the intensive-dose group, with mean cumulative UPCR approximately one-third lower compared with placebo, indicating a sustained reduction in proteinuria [15].

The TULIP_LN study has significant methodological limitations that should be taken into account when interpreting data. First of all, the primary endpoint: the change in UPCR at week 52 was not achieved, as the change in its value was comparable in both groups of patients receiving anifrolumab and in the placebo group. In addition the sample size was limited. It is also worth considering that the favourable results mainly concerned the intensified dosing regimen, while the standard anifrolumab dosing regimen sometimes comparable to or worse than placebo [12].

The two-year follow-up of the TULIP-LN study should be interpreted with caution, as the group of patients eligible for the study was selected- only patients who achieved a renal response and met the GCS reduction criteria were eligible. This may lead to an overestimation of the response in the general population [15].

3.3 Safety and tolerance

In the TULIP-1, the overall safety profile of anifrolumab was comparable to placebo and consistent with findings from the phase 2 programme. Serious adverse events occurred in 14% of patients receiving anifrolumab 300 mg, 11% of those receiving 150 mg, and 16% patients in the placebo group [10].

In the TULIP-2 study, adverse events were reported in 159 of 180 patients receiving anifrolumab and in 153 of 182 patients receiving placebo. The most commonly reported adverse reactions were upper respiratory tract infections, rhinitis and pharyngitis, infusion- related reactions, bronchitis and herpes zoster. Serious adverse events occurred in 8.3% of patients treated with anifrolumab compared with 17% of those receiving placebo. Serious SLE flares were less frequent in the anifrolumab group (1 vs 6 cases). Treatment was discontinued due to adverse events in 2.8% of patients receiving anifrolumab and in 7.1% of patients in the placebo group. One death due to pneumonia was observed in a patient receiving anifrolumab. Particular attention should be paid to the adverse effect of herpes zoster, which occurred in 7.2% of all patients receiving anifrolumab and in 1.1% of patients in the placebo group [11].

In the TULIP-LN study, any adverse event occurred in 95.6% of patients receiving anifrolumab at the standard-dose, 92.2% of patients receiving the intensified dosing regimen of anifrolumab, and 89.8% of patients in the placebo group. Adverse events occurring more frequently in both groups receiving anifrolumab compared to placebo were: Herpes Zoster, urinary tract infections and influenza. Serious adverse events were reported in 22.2% of patients treated with the standard dose, 17.6% of patients treated with the intensified dosing regimen and 16.3% of patients in the placebo group. No deaths were reported during treatment. One fatal vascular neurological adverse event occurred in the standard-dose group during the follow-up period. Due to adverse events, treatment was discontinued in 11.1%-12.2% of patients in all groups. Influenza and herpes zoster occurred more frequently in the anifrolumab treated groups than in the placebo group. Herpes zoster occurred in 20.0% of patients receiving the standard dose, 13.7% of patients receiving the intensified dosing regimen and 8.2% of patients in the placebo group [12].

In the second- year extension of the TULIP-LN study, the safety profile of anifrolumab remained consistent with that observed during the first year of treatment. During the 2-year study period, 11.8% of patients receiving the intensified dosing regimen of anifrolumab, 11.1% of patients receiving the standard dose of anifrolumab and 12.2% of patients in the placebo group discontinued treatment due to adverse events. No deaths were reported during the entire

treatment period, except for the death during follow-up period mentioned before. Herpes zoster and influenza were common in patients receiving anifrolumab than in patients in the placebo group. The incidence of adverse events and serious adverse events decreased in the second year compared with the first year, and serious infections were rare. Opportunistic infections were not observed, only two cases of herpes zoster occurred in the second year [15].

Overall, anifrolumab demonstrated an acceptable safety profile in clinical trials, with the most common adverse events being infections, particularly herpes zoster. Notably, both efficacy and safety require further verification in larger and longer- term studies with appropriate endpoints.

IV. Therapeutic prospects and clinical context.

4.1 Comparison with other biological therapies.

Belimumab, recombinant human monoclonal antibody is the only FDA-approved biological drug for SLE and LN. According to the KDIGO 2021 guideline, standard induction therapy in SLE includes glucocorticoids combined with either mycophenolate or low- dose intravenous cyclophosphamide. Belimumab is a potential add-on therapy based on BLISS-LN results [5]. Similarly, in the EULAR 2023 recommendations, belimumab may be considered as an adjunct to standard therapy for active lupus nephritis [7]. Belimumab inhibits the action of B-cell stimulating factor (BLyS), a cytokine that promotes the survival and differentiation of B cells, including autoreactive B-cell populations. The biological medicine has been approved for patients with active autoantibody- positive SLE who are at least 5 years old [8]. The clinical effects of belimumab were demonstrated in the phase III BLISS-LN study, where significantly more patients in the belimumab group had a primary efficacy renal response (43%) and a complete renal response (30%) compared to the placebo group with standard therapy (32%;20%) [8].

Anifrolumab has not yet been incorporated into treatment guidelines for lupus nephritis. Evidence for the usefulness of anifrolumab in LN was presented in the phase II TULIP-LN study, in which patients with active proliferative lupus nephritis receiving standard therapy with MMF and GCS were divided into three groups: intensified treatment with anifrolumab, standard dose of anifrolumab and placebo. During the continuation of the study up to year 2, it was observed that both anifrolumab regimens demonstrated a larger improvement in eGFR than in the placebo group. A reduction in GCS dosage from at least 20mg/day to 5mg/day or less between weeks 80 and 104 occurred more frequently in the intensified-dose group, followed by the placebo and standard-dose groups. The highest proportion of patients who achieved both a complete renal response and successful glucocorticoid tapering was observed in the intensified-dose group [12,15].

The summary of available data suggests the different roles of both biological drugs in th treatment of lupus nephritis. Belimumab has been supported by phase III trials, on the basis of which it has been included in the latest recommendations as an add- on therapy for patients with active proliferative lupus nephritis. Anifrolumab has shown promising results in phase II trials, but remains in the research phase for use in patients with lupus nephritis, awaiting confirmation of efficacy and safety in phase III trials.

4.2 Directions for future research.

The results of the phase II TULIP-LN trial and its two-year follow-up provided evidence suggesting the potential role of anifrolumab in the treatment of lupus nephritis. Further studies involving larger patient groups are needed to confirm efficacy, optimise dosing regimens and evaluate the long-term effects of therapy [12,15].

The IRIS study is a phase III, multinational, randomized, double-blind study to evaluate the efficacy and safety of anifrolumab as an add-on therapy in patients with active proliferative Class III or Class IV LN. Primary end point is difference in proportion of participans with CRR in anifrolumab group compared with placebo group. The total duration of the study is estimated to be approximately 116 weeks, including both the qualification phase and follow-up visits. Approximately 360 patients will be randomised in a 1:1 ratio to receive either anifrolumab or placebo in combination with mycophenolate mofetil and glucocorticosteroids. The results of the IRIS study will form the basis for decisions on the possible inclusion of anifrolumab in future treatment recommendations for lupus nephritis [16].

Long-term safety remains an important aspect of further research, despite the reduction in adverse events in the two-year follow-up of TULIP-LN. Both the duration of observation and the size of the group are insufficient for a full assessment of the risk associated with chronic use of anifrolumab. The long-term effects of therapy need to be evaluated in future studies.

V. Conclusions

The TULIP-LN study and its 2-year follow-up showed that anifrolumab may have a beneficial effect on the course of lupus nephritis, especially in an intensive dosing regimen. Despite not achieving the primary endpoint of UPCR change at week 52, the study showed that the intensive regimen in particular was associated with significantly better results compared to placebo. In the group of patients receiving an intensified anifrolumab dosage regimen, the following was observed:

- a higher percentage of complete renal response at week 52 compared to placebo (45.5% vs 31.1%);

- a higher percentage of patients who maintained a reduction in oral glucocorticoid dosage to ≤7.5 mg/day compared to placebo (55.6% vs 33.3%);
- a higher percentage of complete renal response at week 104 compared to placebo (25% vs 17.8%);
- improvement in estimated glomerular filtration rate was greater in both anifrolumab groups compared to placebo;
- a higher percentage of patients who achieved reduction in GCS dosage from ≥20 mg/day to ≤5 mg/day during weeks 80-104 compared to placebo (36.1% vs 30.3%);
- greater reduction in non-renal SLEDAI-2K scores in both groups receiving anifrolumab;
- decrease in anti-dsDNA antibody titres, increase in C3 concentration were more pronounced in the high-dose regimen;
- lower cumulative proteinuria throughout the 104- week observation [12,15].

Based on the above results, it can be concluded that anifrolumab administration, particularly in an intensified regimen, may potentially improve renal response and enable more effective reduction of oral GCS administration. Due to the small size of the study population and the short duration of the phase II study, confirmation in a phase III study is needed.

In clinical trials, anifrolumab demonstrated an acceptable safety profile in patients with lupus nephritis associated with SLE. The most commonly reported adverse events were upper respiratory tract infections, rhinopharyngitis, infusion-related reactions and bronchitis. The most significant adverse effect is an increased risk of herpes zoster infection which occurred in 7.2% of patients receiving anifrolumab in the TULIP-2 study, compared to 1.1% of patients in the placebo group [11]. In the TULIP-LN study, in addition to adverse reactions in the form of herpes zoster, influenza, more frequent urinary tract infections were also observed. In TULIP-LN, herpes zoster occurred in 20% of patients receiving standard dose, 13.7% of patients receiving the intensified dosing regimen and 8.2% of patients in the placebo group [12]. During the 2-year follow-up of the TULIP-LN study, the adverse event profile was similar. These data suggest that anifrolumab has an acceptable safety profile, with a predominant increase in risk of infections, particularly herpes zoster.

Anifrolumab, a drug that blocks type I interferon receptors, is a promising therapeutic strategy for lupus nephritis. The results of the TULIP-LN phase II trial indicate potential benefits, especially when using an intensified dosing regimen. However, the data available to date are insufficient to determine its ultimate clinical role; this will be possible once the results of the ongoing phase III IRIS trial are available.

Disclosures

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