International and multidisciplinary expert recommendations for the use of biologics in systemic lupus erythematosus


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International and multidisciplinary expert recommendations for the use of biologics in systemic lupus erythematosus

Authors
Jean-François Kleinmann¹, Florence Tubach², Véronique Le Guern³, Alexis Mathian⁴, Christophe Richez⁵, David Saadoun⁶, Karim Sacre⁷, Jérémy Sellam⁸, Raphaèle Seror⁹, Zahir Amoura⁹, Emmanuel Andres¹⁰, Sylvain Audia¹¹, Brigitte Bader-Meunier¹², Gilles Blaison¹³, Bernard Bonnotte¹¹, Patrice Cacoub⁶, Sophie Caillard¹⁴, Laurent Chiche¹⁵, Olivier Chosidow¹⁶, Nathalie Costedoat-Chalumeau³,⁵, Claire Daïen¹⁷, Eric Daugas¹⁸, Nairouz Derrêche¹, Andrea Doria¹⁹, Olivier Fain²⁰, Fadi Fakhouri²¹, Dominique Farge²², Cem Gabay²³, Sylvie Guillot², Eric Hachulla²⁴, Najia Hajjaj-Hassouni²⁵, Mohamed Hamidou²⁶, Frédéric A. Houssiau²⁷, Noémie Jourde-Chiche²⁸, Isabelle Koné-Paut²⁹, Aïcha Ladjouz-Rezig³⁰, Olivier Lambotte³¹, Dan Lipsker³², Xavier Mariette⁹, Nicolas Martin-Silva³³, Thierry Martin³⁴, François Maurier³⁵, Roderich Meckenstock³⁶, Arsène Mékinian³⁷, Olivier Meyer³⁸, Shirine Mohamed³⁹, Jacques Morel⁴¹, Bruno Moulin⁴², Denis Muller-Andrade⁴³, Thomas Papo⁴⁴, Vincent Poindron³⁴, Xavier Puéchal³, Leonardo Punzi³⁹, Pierre Quartier¹², Laurent Sailler⁴¹, Amar Smail⁴², Martin Soubrier⁴³, Agnès Sparsa⁴⁴, Zoubida Tazi-Mezalek⁴⁴,⁵⁵, Leith Zakraoui⁴⁶, Stéphane Zulily⁴⁷,⁵⁴, Jean Sibilia⁴⁸,⁵⁹, and Jacques-Eric Gottenberg⁶⁰,⁶¹; on behalf of the Société Royale Belge de Rhumatologie/Koninklijke Belgische Vereniging voor Reumatologie (Belgian Society of Rheumatology), the Société Française de Rhumatologie (French Society of Rheumatology) and the Société Suisse de Rhumatologie (Swiss Society of Rheumatology), the CRI (Club Rhumatismes et Inflammation), FLEUR (Réseau Français du Lupus), IMIDATE (Immune-Mediated Inflammatory Disease Alliance for Translational and Clinical Research) and FAI2R (Filière Nationale des Maladies Autoimmunes et Autoinflammatoires Rares) networks.

¹ Rheumatology department, Strasbourg university hospital, Strasbourg, France
² Epidemiology and clinical research, AP-HP, Pitié-Salpêtrière hospital, Paris, France
³ Internal Medicine department, AP-HP, Cochin hospital, Paris, France
⁴ Internal Medicine department, AP-HP, Pitié-Salpêtrière hospital, Paris, France
⁵ Rheumatology department, Bordeaux university hospital, University of Bordeaux, Bordeaux, France
⁶ Internal Medicine and Clinical Immunology department, AP-HP, Pitié-Salpêtrière hospital, Paris, France
⁷ Internal Medicine department, AP-HP, Bichat hospital, INSERM U1149, Paris, France
⁸ Rheumatology department, AP-HP, Saint Antoine hospital, INSERM UMR593, DHU i2B, Paris, France
⁹ Rheumatology department, AP-HP, Bicêtre hospital, Le Kremlin Bicêtre, France
¹⁰ Internal Medicine department, Strasbourg university hospital, Strasbourg, France
¹¹ Internal Medicine and Clinical Immunology department, Dijon university hospital, University of Bourgogne Franche-Comté, INSERM UMR1098, FHU INCREASE, Dijon, France
¹² Paediatric Immunology and Rheumatology department of, APHP, Necker hospital, Institut Imagine, Paris, France
¹³ internal Medicine department, Colmar hospital, Colmar, France
¹⁴ Nephrology department, Strasbourg university hospital, Strasbourg, France
¹⁵ Internal Medicine department, Hôpital Européen, Marseille, France
¹⁶ Dermatology department, AP-HP, Henri Mondor hospital, Paris, France
¹⁷ Rheumatology department, Montpellier university hospital, Montpellier, France
¹⁸ Nephrology department, AP-HP, Bichat hospital hospital, Paris, France
¹⁹ Medicine department-DIMED, University of Padova, Padova, Italy
²⁰ Internal Medicine department, AP-HP, Saint Antoine hospital, Paris, France
²¹ Nephrology department, Nantes university hospital, Nantes, France
²² Internal Medicine department, AP-HP, Saint Louis hospital, University of Paris Diderot, Paris, France
²³ Rheumatology department, Geneva university hospital, Geneva, Switzerland
²⁴ Internal Medicine department, Lille university hospital, University of Lille, Lille, France
²⁵ Rheumatology department, El Ayachi university hospital, URAC 30, Faculty of medicine, Salé, Morocco
²⁶ Internal Medicine department, Nantes university hospital, Nantes, France
²⁷ Pôle de maladies rhumatismales, Université Catholique de Louvain, Louvain-la-Neuve, Belgium
²⁸ Nephrology department, AP-HM, Marseille university hospital, University Aix-Marseille, Marseille, France
Corresponding author:
Prof Jacques-Eric GOTTENBERG
jacques-eric.gottenberg@chru-strasbourg.fr
jegotten@gmail.com
Service de Rhumatologie
Centre National de Référence des Maladies AutoImmunes Systémiques Rares
CHU Strasbourg-Hautepierre
1 Avenue Molière
67098 STRASBOURG Cedex
FRANCE

Abstract

Background/Purpose:
Despite conventional immunosuppressants, active and steroid-dependent systemic lupus erythematosus (SLE) represents a therapeutic challenge. Only one biologic, belimumab, has been approved, but other biologics are sometimes used off-label. Given the lack of evidence-based data in some clinical situations encountered in real life, we developed expert recommendations for the use of biologics for SLE.

Methods:
The recommendations were developed by a formal consensus method. This method aims to formalise the degree of agreement among experts by identifying, through iterative ratings with feedback, the points on which experts agree, disagree or are undecided. Hence, the recommendations are based on the agreed-upon points. We gathered the opinion of 59 French-speaking SLE experts from 3 clinical networks dedicated to systemic autoimmune diseases (FLEUR, IMIDIATE, FAI2R) from Algeria, Belgium, France, Italy, Morocco, Switzerland and Tunisia. Represented medical specialities were internal medicine (49%), rheumatology (34%), nephrology (7%), dermatology (5%), pediatrics (3%) and cardiology (2%). Two methodologists and 3 strictly independent SLE expert groups contributed to developing these recommendations: a steering group (SG) (n=9), an evaluation group (EG) (n=28) and a reading group (RG) (n=22). Preliminary recommendations were drafted by the SG, then proposed to the EG. Each EG member rated the degree of agreement from 1 to 9 (1: lowest; 9: strongest) for each recommendation. After 2 rating rounds, the SG submitted a new version of the
recommendations to the RG. With comments from the RG, the SG finalised the recommendations.

Results:
A total of 17 final recommendations were formulated by the SG, considering all agreement scores and comments by the EG and RG members and the two methodologists. These recommendations define the subset of patients who require a biologic; the type of biologics to use (belimumab, rituximab, etc.) depending on the organ involvement and associated co-treatments; what information should be given to patients; and how to evaluate treatment efficacy and when to consider discontinuation.

Conclusion:
Overall, 17 recommendations for the good use of biologics in SLE were formulated by a large panel of SLE experts to provide guidance for clinicians in daily practice. These recommendations will be regularly updated according to the results of new randomized trials and increasing real life experience.

Keywords:
- Lupus
- Biological
- Recommendation

1. Introduction
Systemic lupus erythematosus (SLE) is a severe systemic autoimmune disease that often represents a therapeutic challenge because of diverse manifestations, clinical course and prognosis. Patients with SLE are followed by different specialists because of several organ involvements, and treatments are tailored depending on the disease activity and/or severity of the organ involvement(s), comorbidities, side effects, drug interactions, drug availability, previous treatment and patient preference. Poorly controlled disease drives a vicious circle, with organ damage undermining the long-term prognosis (1-3), triggered itself by persistent disease activity and particularly by corticosteroids abuse (4-10). Hence, the main target in clinical practice is to prevent damage and maintain stable disease control with limited doses of corticosteroids (7, 11).

An evidence-based approach to therapy is desirable, but the actual benefit demonstrated by randomized controlled trials and cohort evaluations of biologics in SLE are still limited (10, 12). Only one biologic, belimumab (13), has been approved to date, but other biologics are sometimes used off-label. The strategy of use of biologics remains a “grey area” in the literature (14-22) because of the limited evidence-based data and the wide range of situations encountered in real-life practice (10). Opinions of highly qualified experts in SLE treatment are essential when data are absent or controversial.

Therefore, we established a set of expert recommendations for the use of biologics in SLE.

2. Methods
2.1 Literature search of available data
To assess the amount of available data, we searched for articles published up to June 2014. This search is synthesized in a published book in which most of the authors contributed. The book is presented in Supplementary Information.

2.2 Definition of the recommendations scope
In light of the available literature, four clinical questions were defined: 1) Which patients might benefit from biologic therapy? 2) Which biologic and co-treatment might be used? 3) Which information should be given to patients? 4) How should the effectiveness of a biologic be evaluated and when should treatment be discontinued?
2.3 Criteria for choice of methodology for elaborating recommendations

We used the method “Recommendations by formalized consensus (RFC)” (23) (see Fig. 1). This method is relevant when at least two of the following conditions are met: 1) absence or insufficiency of a high level of evidence specifically answering the questions; 2) controversy, with the need to identify and select among several possibilities the situations in which a practice is deemed appropriate by an independent panel of experts; and 3) the possibility to break down the theme in easily identifiable clinical situations (lists of indications, criteria, etc.).

In brief, the degree of agreement with each recommendation is formalized, and a recommendation is validated only after consensus has been reached by experts. In case of controversy, proposed recommendations are modified and submitted again to the experts until consensus is reached. This process favors extremes and not just median opinions; if the degree of agreement is not sufficiently strong, proposals are re-worded or may be rejected.

According to the state of the art (available literature and current clinical experience), the Steering Group (SG) drafted 20 preliminary propositions for the defined clinical questions addressed by the recommendations.

2.4 Detailed process of response analysis

Three strictly independent SLE expert groups contributed to these recommendations: an SG, an Evaluation Group (EG) and a Reading Group (RG). Experts scored their degree of agreement from 1 to 9 (1, lowest agreement; 9, strongest agreement; 5, indecision).

The following analysis rules allowed for judging the appropriateness or non-appropriateness of proposals that the SG submitted to the EG and RG for voting on:

- During rating rounds by the EG, a proposal was considered:
  - **Appropriate / non-appropriate (strong agreement):**
    - if the median response was \( \geq 7 \) AND the response distribution was [7-9], the recommendation may be accepted as such, without the need for a second round of scoring;
    - if the median was \( \leq 3 \) AND response distribution was [1-3], the recommendation was rejected as such.
  - **Relative agreement / uncertain (indecision / no consensus):**
    - if the median was \( \geq 7 \) AND the response distribution was [5-9] OR if the median was \( \leq 3.5 \) AND the response distribution was [1-5], the result was *relative agreement*;
    - if the median was 4–6.5 AND the response distribution was [1-9], the result was *indecision*;
    - in all other situations (with at least one extreme value in score distribution), the result was *no consensus*.

In the 3 last cases, the SG had to discuss the recommendation before a second round of scoring.

EG experts had to vote on all propositions submitted to them. During the evaluation stage, the SG requested that EG experts explain their uncertain responses. EG experts who did not discussed their uncertain responses between the first and second evaluation rounds were not allowed to participate in the second evaluation round. The first evaluation round was more conservative because any situation of uncertainty had to be discussed. The second evaluation round allowed, if the EG was at least composed of 16 members, to exclude a maximum of 2 missing or extreme values.

- During the reading step,
  - if \( \geq 90\% \) of the RG response distribution was [5-9] (i.e., the RG confirmed the appropriateness), the recommendation was maintained, and relevant comments were considered to improve the wording;
  - if < 90\% of the RG response distribution was [5-9] (i.e., the RG is undecided or disagrees), the SG offered possible changes based on RG comments, after debate or voting with the EG in case of substantial changes, or rejected the recommendation.
The RG members did not have to vote on all propositions submitted to them but only had to answer those within their field of expertise.

2.5 Recommendations elaboration

SLE experts were recruited from 3 networks dedicated to rare systemic autoimmune diseases of the Club Rhumatismes et Inflammations (CRI), a specialized section of the French Society for Rheumatology (SFR): Filière Nationale des Maladies Autoimmunes et Autoinflammatoires Rares FAI2R (FAI2R), Immune-Mediated Inflammatory Disease Alliance for Translational and Clinical Research (CRI-IMIDIA), and French Lupus Network (FLEUR). Clinician French-speaking SLE experts who agreed to participate in developing the recommendations (60 of 92 contacted) had a proven academic track record and/or long-standing experience in the care of SLE patients at academic centres located in Algeria, Belgium, France, Italy, Morocco, Switzerland and Tunisia. Represented medical specialities were internal medicine (49%), rheumatology (33%), nephrology (7%), dermatology (5%), pediatrics (3%) and cardiology (2%). All the work was coordinated and documented by a project manager, piloted by the SG assisted by two methodologists.

3. Results

Overview of recommendations development (see Table 1):

3.1 Steering step

The SG drafted 20 preliminary propositions that were sent by email to each EG expert for agreement scoring.

3.2 Evaluation step

EG experts scored their degree of agreement from 1 to 9 (1, lowest agreement; 9, strongest agreement; 5, indecision).

- The first evaluation round resulted in 28 individual responses (n=28). Four recommendations had strong agreement (median ≥7; values [7-9]), 2 a fair agreement (median ≥7; values [5-9]), and 14 showed a low agreement: 6 preliminary propositions (30%), mostly related to “patient information” and “effectiveness and discontinuation criteria”, were rated appropriate (strong or fair agreement), and 14 (70%), mostly related to “patient definition” and “biologic and co-treatments”, showed a low agreement*.

From the 20 preliminary recommendations, 9 were retained: 10 were grouped in to 3 recommendations and 1 was rejected, which resulted in 12 propositions* redrafted by the SG, considering the comments made by EG experts and methodologists, before a second round of scoring. Moreover, each EG expert was asked to put forward an oral corticosteroid dependence threshold (mg/day): 21 suggested a median threshold of 10 mg/day (min: 5 mg/day, max: 30 mg/day) and others considered this point not applicable because the effects of corticosteroids vary among patients and by age. A corticosteroid-sparing threshold (after 6 months of treatment) was also polled among EG members: 13 suggested a median decrease of at least 50% of the initial dose (min: 10%, max: 50%) and others considered this definition too restrictive because it should be relative to the type and severity of the disease.

- The second evaluation round collected 19 individual responses (n=28). Three recommendations had strong agreement (median ≥7; values [7-9]), 4 a fair agreement (median ≥7; values [5-9]), and 5 a low agreement. By excluding 2 extreme values per proposal voted, as permitted by the second-round rules, 9 recommendations with strong agreement and 3 with fair agreement were obtained: if all redrafted propositions were appropriate, 9 (75%), mostly related to “patient definition”, “patient information” and “effectiveness and discontinuation criteria”, showed strong agreement, and 3 (25%), mostly related to “biologic and co-treatments”, showed fair agreement*. 

* Final versions of recommendations are available online at the CRI-IMIDIA and FAI2R websites.
From the 12 last propositions, 8 were retained: 2 were shifted in 3 recommendations and 2 shifted in 2 recommendations, which resulted in **18 initial recommendations** established by the SG, considering all EG group remarks on the form and substance.

### 3.3 Reading step

Then the 18 initial recommendations were sent by email to the RG members, who scored and commented on each initial recommendation. In the reading stage, 22 individual responses for 18 initial recommendations were obtained (n=22). In all, 14 recommendations had strong agreement (≥ 90% values [5-9], with relevant form comments) and 4 had some indecision or disagreement (values [5-9] 77–82%, with form and substance comments); 14 initial recommendations (78%), mostly related to “patient definition,” “patient information” and “effectiveness and discontinuation criteria”, were confirmed, but 4 (22%), mostly related to “biologic and co-treatment”, showed uncertainty. From the 18 initial recommendations, 1 was shifted in 2 recommendations and 2 were rejected (when expert’s final agreement could not be reached), which resulted in **17 final recommendations** established by the SG, considering all expert remarks to achieve final consensus.

*The different versions of the recommendations (preliminary and redrafted propositions, initial and final recommendations) are in Supplementary Information.

### 3.4 Finalization of the recommendations

All 17 final recommendations were redrafted by the SG, considering all SG/EG and methodologist’s comments (see Table 2, Figs. 2 and 3).

### 4. Discussion

A large panel of SLE experts formulated 17 recommendations for the good use of biologics in SLE to provide guidance for clinicians in daily practice.

The main advantages of the method to develop the recommendations are 1) the strict independence between the SG, which formulated proposals for voting, and the EG and RG, which judged the appropriateness of the proposals, thus avoiding one group as judge and jury; 2) the ability to identify the degree of agreement or indecision among experts by selecting from several elementary, complementary or contradictory situations for which an indication is deemed appropriate, inappropriate or uncertain; and 3) the capacity to formalize expert advice without requiring a perfect convergence of opinions.

The main limitation of the method is the number of expert groups that should be constituted. This limitation is particularly relevant when the theme is extended to various fields of expertise requiring the participation of a large number of medical specialties. Therefore, we included in the task force all the different specialists involved in the daily care of lupus patients (internal medicine practitioners, rheumatologists, nephrologists, dermatologists, pediatricians). The high technical aspect of these recommendations did not allow for an involvement of patient representatives in the working groups. Indeed, these recommendations target mostly specialized physicians. From the patient’s perspective, when several equivalent care options are available, patient “preferences” are usually considered at the time of care implementation (Cf. R11).

The individual recommendations are not structured by importance but rather by a logical sequence facilitating their use by clinicians in daily practice and their updating: 1) which patients can benefit from a treatment with a biologic, 2) what biologic treatment and co-treatment to use, 3) what information to give to patients, and 4) how to judge the effectiveness of a biologic and when to stop treatment.

The first objective of these recommendations was to define the target population for the use of biologics in SLE. As there is no definition for refractory SLE, these patients should be defined as the failure to achieve disease control using the standard of care after adequate pharmacokinetic exposure to drugs has been assessed (7). Three parameters were used to define the population of “refractory” or corticodependent patients: 1) disease activity, 2) previous use of immunomodulatory and immunosuppressive drugs, and 3) corticodependence. Of note, no consensus was reached on the use of a specific disease activity score such as SLEDAI, BILAG, or SRI in daily practice, confirming there
is no gold standard (24). Regarding the previous use of immunomodulatory drugs, the final consensus was that patients should be refractory to hydroxychloroquine (poor adherence to hydroxychloroquine therapy was emphasized (10), along with the usefulness of monitoring hydroxychloroquine blood levels (25)), considered an immunomodulatory rather than immunosuppressive drug, and refractory to at least two successive other immunosuppressive drugs (e.g., methotrexate and azathioprine). The recommendation (R2) to initiate a biologic only after failure of two conventional immunosuppressive drug differs from the label of the only marketed biologic in SLE, belimumab (authorized after conventional therapy failure i.e. hydroxychloroquine and corticosteroids and/or immunosuppressor, without a number of previous tested immunosuppressors being specified). Failure of two immunosuppressive drugs before initiation of a biologic does not concern refractory SLE with central nervous system involvement, a situation when rituximab can be used after the failure of cyclophosphamide (26). Although the threshold of corticdependence was controversial, consensus was reached on the dose of 10 mg/day prednisone, but the experts insisted that this threshold should depend on patient comorbidities.

The second important objective was to recommend the use of a specific biologic depending on organ involvement and to discuss the use of co-medications. Belimumab was considered the first biologic to use when clinical involvement corresponds to the inclusion criteria of the belimumab pivotal trials (mainly skin, mucosal and articular complications and absence of kidney and central nervous system involvement). For patients with renal complications or autoimmune cytopenias, despite the negative results of the randomized placebo-controlled LUNAR and EXPLORER trials (27, 28), the experts favored rituximab as the first biologic to use in light of the large amount of positive observational evidence (open trials and registries) (29-33). This position needs to be reevaluated in light of the results of the ongoing randomized trials evaluating belimumab and rituximab in renal lupus (7, 34). Interestingly, consensus was not reached on the use of abatacept, with negative results from two randomized trials but positive observational evidence (35-37), like rituximab, which is being evaluated in phase III randomized trials RING (NCT01673295) and RITUXILUP (NCT01773616). Consensus was not reached on the use of tocilizumab or anti-TNF agents, two drugs for which limited experience is available literature (7, 38-40). However, experts agreed that abatacept, tocilizumab, anti-TNF agents or rituximab could be prescribed for patients with rheumatoid arthritis and concomitant SLE (“rhupus”).

Regarding co-treatments, the discussion was controversial regarding the need to use an immunosuppressive drug concomitantly with the biologic prescribed. Some experts argued that no specific data are available to indicate an improved response in patients with SLE receiving an immunosuppressive drug and a biologic as compared to biologic monotherapy. This recommendation does not concern hydroxychloroquine, considered an immunomodulatory rather than immunosuppressive drug, which can be continued in conjunction with a biologic, if well tolerated, because it prevents severe complications of the disease and lupus flares (41). Of course, as stated in recommendation 9, the combination of two immunomodulatory biologics is not recommended. This recommendation does not concern denosumab, a biologic that can be used in lupus for osteoporosis and might be associated with an immunosuppressive biologic.

The third important objective was to define the aim of prescribing a biologic in terms of disease activity control, a corticosteroid-sparing effect, and to propose how to monitor the treatment efficacy and safety. The controversies on this objective were similar to those for defining the target population. Again, the consensus was to avoid mentioning only one specific disease activity score, because such scores are not used on a systematic basis in daily practice. Therefore, the patient and physician’s global assessment were considered in that recommendation.

Consensus was reached on a decrease in prednisone dose ≥ 50% if the initial dose was > 10 mg/day, to reach a final dose ≤1 mg/10 kg prednisone equivalent. This threshold was agreed upon because a greater daily dose is associated with corticosteroid-related damage in lupus (5). The evaluation term was defined at 6 months, but this follow-up might also depend on organ involvement and the biologic used. For example, renal response might take a longer time but usually begins within 6 months after rituximab infusions.

The fourth important objective was to address specific situations in current practice usually excluded in randomized clinical trials, mainly antiphospholipid syndrome, pregnancy, and vaccinations (20, 42). Previous treatment, information given to patients and when needed, the advice of reference centers for autoimmune diseases, were emphasized in these recommendations.
These recommendations will be regularly updated according to the results of new randomized trials and increasing real-life experience.

5. Conclusion

We report 17 recommendations for the use of biologics in SLE that were developed with a formalized consensus of an international panel of experts. These recommendations are based on the most recent evidence in lupus management and discussions by a large and broadly international task force. The recommendations synthesize the current approaches to lupus treatment. The task force is convinced of the importance to disseminate these recommendations. It hopes that following these recommendations (i.e., defining the target patient population, the treatment target, and assessing disease activity regularly) will optimize the overall outcome in lupus patients.

6. Acknowledgments

These recommendations for the use of biologics in SLE were developed by multidisciplinary panels of experts on behalf of the Club Rhumatismes et Inflammation. French national networks focused on rare systemic autoimmune diseases contributed to this work by identifying SLE experts in France, Europe and North Africa and by the contribution of network-affiliated methodologists.

- **FAI2R** (*Filière Nationale des Maladies Autoimmunes et Autoinflammatoires Rares*), including 7 referee centres, 73 competence/expert centers, 10 French associations in the field of rare diseases (also involved in Eurodis), and 8 national French scientific societies. It covers more than 65,000 patients with rare autoimmune or autoinflammatory diseases in France.

- **IMIDIATE** (*Immune-Mediated Inflammatory Disease Alliance for Translational and Clinical Research*), a clinical research infrastructure funded by the French-Clinical Research Investigation Network (F-CRIN) that aims to facilitate clinical research in immune-mediated inflammatory diseases by bringing together French investigators and facilitating their participation in large-scale research protocols, with a culture of quality and excellence.

- **FLEUR** (*Réseau Français du Lupus*), including 5 referee centres, 22 competence centres, 2 French associations and several expert centres in SLE.

These recommendations were endorsed by the Société Royale Belge de Rhumatologie/Coninklijke Belgische Vereniging voor Reumatologie (*Belgian Society of Rheumatology*), the Société Française de Rhumatologie (*French Society of Rheumatology*) and the Société Suisse de Rhumatologie (*Swiss Society of Rheumatology*).

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7. References


**Table 1:** Overview of recommendation development by SLE expert independent groups

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**Table 2:** Recommendations for the use of biologics in SLE (final version)

**Which patients can benefit from treatment with biologics**

R1 With disease activity persistence, despite lupus conventional treatment or corticosteroid dependence (usual threshold ≥ 10 mg/day prednisone equivalent), dose discussed according to patient comorbidities and corticosteroid-related adverse events, actual patient adherence to treatment must be checked, before concluding treatment ineffectiveness, by clinical examination and by assessing, for example, blood levels of hydroxychloroquine.

R2 With active or corticosteroid-dependent lupus, despite hydroxychloroquine treatment and at least two successive immunosuppressive therapies (e.g., methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide), a biologic treatment can be prescribed.

R3 An antiphospholipid syndrome (APS) associated with lupus is not an indication for treatment with biologics but can be discussed in case of the following:

- Autoimmune thrombocytopenia (< 25 G/l) associated with APS and/or haemorrhagic manifestations and refractory to usual treatments of immunological thrombocytopenia and/or a particular situation (surgery, bleeding requiring temporary discontinuation of anticoagulants, need to maintain platelet count ≥ 50 G/l because of sport or professional activity at risk of trauma).

- Catastrophic APS (CAPS)

R4 A biologic treatment should not be used during pregnancy unless in an absolute medical necessity (disease activity threatening vital prognosis and/or compromising pregnancy continuation, despite lupus treatments authorized during pregnancy) after systemic consultation in a reference centre for teratogenic agents to evaluate the safety of the proposed biologic.

R5 If a patient is exposed to a biologic treatment during pregnancy, a tight and specialized monitoring, including foetal echography, should be performed and the situation reported to a pharmacovigilance centre and a reference centre for teratogenic agents. The decision to stop a biologic should take into account disease activity, possibility of alternative treatments authorized during pregnancy, and type of biologic used.

**What biologic treatment and co-treatment to use**

R6 In refractory and corticosteroid-dependent disease forms (see definition in Recommendation 2), in the absence of kidney or central nervous system involvement or severe autoimmune thrombocytopenia, belimumab can be used.

R7 In refractory and corticosteroid-dependent forms of kidney or central nervous system involvement or severe autoimmune thrombocytopenia, rituximab can be used as the first biologic.

R8 A conventional immunosuppressant does not systematically need to be associated with a biologic.

R9 The combination of two immunomodulatory biologics is not indicated.
R10  In rhupus situations (rheumatoid arthritis and concomitant lupus), anti-TNF therapy, abatacept, rituximab or tocilizumab can be used, keeping in mind the potential risk of lupus flare with anti-TNF agents and neutropenia with tocilizumab.

What information to give to patients

R11  At the time of biologic initiation, clinicians should explain the reasons for the prescription, expected benefits, potential adverse events, monitoring modalities and what to do in case of an adverse event, such as an infection. The need to discontinue a biologic before surgery should also be explained.

R12  Before initiating a biologic, clinicians should propose an update of vaccines according to current recommendations in the general population. If a live attenuated vaccine is required (e.g., yellow fever, rubella, mumps and measles), the vaccine must be given at least 1 month before initiation of the biologic (live attenuated vaccines are contraindicated during biologic treatments). Hepatitis B and C serology should also be controlled. A hepatitis B pre-emptive anti-viral treatment should be discussed in case of non-seroconverted hepatitis B. It is highly recommended, before initiating a biologic treatment, to propose vaccination against pneumococcus and seasonal influenza. If a therapeutic emergency requires biological initiation before vaccination, non-live vaccines may also be used, as soon as possible after biological initiation, although their effectiveness may be diminished.

R13  In women of childbearing age, effective contraception is required and must be prescribed for the whole treatment period. This contraception should be continued after biologic discontinuation for five half-lives of the biologic agent. If pregnancy is desired, it must be scheduled and treatments must be revised accordingly (see Recommendations 4 & 5).

How to judge the effectiveness of the biologic and when to stop treatment

R14  The therapeutic goals in the 6 months after the initiation of a biologic treatment are as follows:

- Decrease in disease activity, particularly regarding target organ(s), evaluated by a validated disease activity score and according to disease activity evaluated by the patient and the physician.
- Oral corticosteroid discontinuation or corticosteroid-sparing (decrease ≥50% of the initial dose if the initial dose was >10 mg/day, to reach, if possible, a final dose ≤1 mg/10 kg prednisone equivalent).

R15  The monitoring of a biologic treatment should be clinical and based on laboratory examinations. Effectiveness should be assessed by validated disease activity scores. Tolerance should be assessed, with particular attention paid to the risk of infections. Safety should be assessed at each administration, both clinically and with laboratory examinations. With serious adverse events, the treatment should be stopped. According to the imputability of the adverse event to biologic treatment, the severity of the adverse event, its reversibility, the benefit/risk ratio for the patient, re-treatment or definitive discontinuation should be discussed.

R16  The safety and efficacy of a biologic treatment should be evaluated on a regular basis, at least at 1, 3 and 6 months after biologic initiation. In the absence of a documented clinical effectiveness at 6 months (see Recommendation 14), the biologic treatment should be discontinued.

R17  If a biologic treatment is maintained beyond 6 months, a re-evaluation (at least bi-annually) by a physician experienced in SLE management, possibly in conjunction with a reference centre for systemic autoimmune diseases, should be performed to confirm its maintenance.
Fig. 1: Process of formalized consensus of experts to elaborate recommendations for the use of biologics in SLE.
Fig. 2: Distribution of the recommendations among the four domains
Fig. 3: Algorithm for the choice of biologic depending on organ(s) involvement and coexisting diseases

Recommendations for biologics in SLE
Take home messages

- 17 recommendations for the good use of biologics in SLE were formulated by a large panel of SLE experts
- These recommendations define:
  - The subset of patients who require a biologic
  - The type of biologics and co-treatment to use
  - What information should be given to patients
  - How to evaluate treatment efficacy and when to consider discontinuation