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### Learning Objectives

- Describe the evidence base for current cyclophosphamide-based regimens
- Discuss the advantages and disadvantages of using cyclophosphamide-based regimens
- Explain how cyclophosphamide might be used in combination with newer therapies

## 03 TOP 10 TIPS REGARDING PATIENT ADHERENCE TO HYDROXYCHLOROQUINE

Nathalie Costedoat-Chalumeau. *CHU Paris Centre – Hôpital Cochin, Paris, France*

10.1136/lupus-2022-la.3

Adherence is defined as ‘the extent to which a person’s behaviour coincides with medical or health advice’. Non-adherence to therapeutic regimens is a common and expensive problem in patients with chronic diseases including systemic lupus erythematosus (SLE) and is associated with a higher risk of flares, morbidity, hospitalisations and poor renal outcomes.<sup>1–2</sup> Non-adherence is also very difficult to evaluate.<sup>3–5</sup>

Hydroxychloroquine (HCQ), an important medication in SLE with an excellent benefit:risk ratio, has a long half-life and it can be measured in blood. Undetectable or very low levels of blood HCQ is then a simple, objective and reliable marker of non-adherence in SLE patients.<sup>1–4–5</sup>

Levels of HCQ and then HCQ non-adherence should be routinely and repeatedly assessed. If severe non-adherence is unmasked, a non-judgmental and open discussion must take place to improve adherence as much as possible. This task is not simple, but particularly important and some tips will be discussed (table 1).<sup>5</sup>

### Abstract 02 Table 1 Addressing medication non-adherence in clinical practice

Remember that non-adherence is the rule and perfect adherence the exception.  
 Improve your diagnostic skills to unmask non-adherence.  
 Always ask open questions.  
 Use objective methods to detect non-adherence, such as measurement of blood hydroxychloroquine levels.  
 Try to understand the reasons for non-adherence.  
 Explain but listen first.  
 Set-up a tailored-management plan.

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### Learning Objectives

- Recognise the frequency and consequences of non-adherence
- Describe methods to evaluate non-adherence
- Analyse blood hydroxychloroquine levels
- Improve the way we discuss non-adherence with our patients

## Opening session (live-streamed with external Q&A)

### Debate

## 04 THE MATTER OF THE DEBATE: LLDAS IS AN EXCELLENT OUTCOME MEASURE, BUT DOES IT REALLY CAPTURE PATIENTS WITH TRUE LDA?

Ronald van Vollenhoven. *Amsterdam University Medical Centers, and Amsterdam Rheumatology and Immunology Center, The Netherlands*

10.1136/lupus-2022-la.4

Accurate definitions of disease states can be very helpful in care, education and research. During recent years, definitions of low disease activity and remission in systemic lupus erythematosus (SLE) have been developed, tested and published. The definition Low Lupus Disease Activity State (LLDAS) was extensively validated and has already been utilized in several studies and clinical trials. However, some uncertainties remain. Does this definition define patients whose disease does truly have a low level of activity? Or conversely, can patients whose disease activity really is low be ‘missed’ by this definition? And if so, what would the consequences of that be. These questions will be addressed in this year’s debate at the 11th Annual Meeting of the Lupus Academy.

### Learning Objectives

- Explain the importance of having definitions of lupus disease states
- Describe the recent development of the LLDAS
- Demonstrate understanding that some questions remain around the LLDAS

## 05 LLDAS IS AN EXCELLENT OUTCOME MEASURE, BUT DOES IT REALLY CAPTURE PATIENTS WITH TRUE LDA?

### YES

Eric Morand. *Monash University, Melbourne, Australia*

10.1136/lupus-2022-la.5

The deployment of treat-to-target approaches requires the identification of feasible, attainable endpoints, that are empirically associated with improved patient outcomes. While remission is the goal of care, the AsiaPacific Lupus

Collaboration set itself the task in 2013 of developing and validating a measure of low disease activity (LDA) for SLE, on the basis that remission as defined at that time was rarely attained, with the aspiration that a less stringent goal might still be associated with improved outcomes despite higher attainability. The use of careful consensus methodology yielded the Lupus Low Disease Activity State (LLDAS), which has now been shown in multiple independent cohorts to be attainable, but also highly protective from flare, damage accrual, low quality of life, and mortality. Validation studies include a multicentre prospective study, which confirmed that most definitions of remission were much less attainable but no more protective.

Attainability is important, and the combination of strong protection and good attainability has seen LLDAS deployed in many clinical trials, both post hoc and a priori, where it has discriminated active treatment from placebo in at least five trials.

### Learning Objectives

- Discuss why, while remission is the goal of care for systemic lupus erythematosus, low disease activity may be more attainable and more pragmatic
- Describe how LLDAS is a thoroughly validated treat-to-target endpoint for SLE
- Explain why, compared with remission, the greater attainability of LLDAS enhances its performance as a clinical trial endpoint

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### LLDAS IS AN EXCELLENT OUTCOME MEASURE, BUT DOES IT REALLY CAPTURE PATIENTS WITH TRUE LDA?

NO

Andrea Doria. University of Padova, Italy

10.1136/lupus-2022-la.6

A precise definition of low disease activity (LDA) in systemic lupus erythematosus (SLE) is crucial for managing patients according to a T2T strategy.<sup>1</sup> Lupus low disease activity state (LLDAS) was proven to be a valid outcome measure,<sup>2</sup> since its achievement is associated with a significant decrease in disease flares and damage accrual, as well as with improved HR-QoL.

Some pitfalls, however, may affect the definition of LLDAS:

1. LLDAS is not aligned with the DORIS definition of remission, particularly in the most important item - SLEDAI. Indeed, SLEDAI $\leq$ 4 (including serology) is considered in the definition of LLDAS, by contrast clinical SLEDAI=0 is included in the DORIS definition. We know that a significant proportion of patients with SLEDAI $\leq$ 4 has a clinical SLEDAI=0, since they are patients with serologically active clinical quiescent disease (SACQ). As a consequence, there is a great overlap between LLDAS and DORIS remission, i.e. the majority of patients in LLDAS are also in remission on therapy, according to the DORIS definition of remission.<sup>3</sup> Thus, LLDAS cannot discriminate between patients in LDA and those in remission.<sup>4</sup>

2. The item that could theoretically distinguish between remission and LLDAS is physician global assessment (PGA), which has a cut-off of  $\leq 0.5$  for remission and  $\leq 1.0$  for LLDAS. It is, however, very difficult to predict the phenotype of patients with a PGA in between 0.5 and 1.0, and a poor inter-rater and intra-rater reliability of PGA has been recently confirmed in a meta-analysis, which highlighted the need for PGA standardisation.<sup>5</sup> Notably, in a recent paper testing different definitions of remission, PGA did not increase the performance of clinical SLEDAI=0 in predicting damage progression.<sup>6</sup>
3. Thus, the remaining item able to distinguish patients in remission from those in LLDAS is glucocorticoid intake:  $\leq 5$  mg in remission according to the DORIS definition and  $\leq 7.5$  mg in LLDAS. It has, however, been shown that the great majority of patients in LLDAS receive a dosage of prednisone  $\leq 5$  mg/day; moreover, the habit of prescribing prednisone largely varies among rheumatologists,<sup>7</sup> and cannot be easily standardised.

In addition, the major reason why LLDAS cannot capture patients in 'true' LDA is that it is based on the SLEDAI score, i.e. a binomial disease activity index that measures disease activity in each organ domain in terms of 'present' or 'absent', but it is not able to discriminate the level of disease activity within any single organ domain.

A new disease activity index named SLE-DAS (<http://sle-das.eu>) has recently been proposed and validated,<sup>8</sup> which measures disease activity in a continuous fashion and, thus, is more sensitive to clinical changes compared with the SLEDAI. The SLE-DAS includes some items that are not considered in the SLEDAI, namely lupus enteritis, cardiac and pulmonary manifestations and haemolytic anaemia. In addition, some items that are binomial in the SLEDAI were turned into continuous in the SLE-DAS, including arthritis, proteinuria, thrombocytopenia, and leukopenia. The SLE-DAS cut-offs for defining remission and LDA have recently been derived and validated.<sup>9 10</sup>

### Learning Objectives

- Discuss the hurdles in defining low disease activity in SLE and the pitfalls of LLDAS
- Discuss why LLDAS does not capture patients with 'true' LDA
- Explain lupus LDA in clinical practice, and discuss other instruments that might identify patients in LDA better than LLDAS

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