

What are the topics you care about making trials in lupus more effective? Results of an Open Space meeting of international lupus experts

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ABSTRACT

Despite promising candidates for new therapeutic options in the treatment of systemic lupus erythematosus (SLE), many clinical trials have failed in the past few years. The disappointing results have been at least partly attributed to trial designs. With the aim of stimulating new developments in SLE trial design, an international open space meeting was held on occasion of the European Lupus Meeting 2018 in Duesseldorf, Germany about ‘What are the topics you care about for making trials in lupus more effective?’. The Open Space is a participant-driven technology, where the discussion topics and schedule are selected during the meeting by all participants and discussion rounds are led by the people attending encouraging active contributions. Eleven topics were selected for further discussion, of which 6 were voted to be more intensively discussed in two consecutive rounds. Major topics were the optimal handling of glucocorticoids in clinical trials, the improvement of outcome measures, reducing or controlling the placebo response and the identification of biomarkers and stratification parameters. Further, the importance of local and international networks was emphasised. By networking, collaborations are facilitated, patient recruitment is more efficient and treatment can be harmonised thus lead to more successful SLE trials. Further discussions are needed to substantiate the results and develop new trial designs.

INTRODUCTION

During the past few decades, the expectations of living with systemic lupus erythematosus (SLE) changed substantially for both patients and their treating physicians. With life-threatening consequences of acute episodes becoming less common due to better therapeutic options and improved medical care, SLE is now considered a chronic condition, although with a substantial disease burden

and risk of impact on lives.^{1 2} However, due to the disease and adverse effects of therapies, life-threatening manifestations for some patients or damage and premature death for most, are still real.^{3 4}

Across the same period of time, physicians have observed the tremendous efficacy of biologicals and target-specific drugs in the treatment of other rheumatic diseases, such as rheumatoid arthritis or spondyloarthritis and have hoped for this wave of innovation to spill over to SLE, for similar results. So far, however, only one drug of many, belimumab, has been approved for use in SLE (with failure).^{5–7} A few novel drugs have now completed successful phase III trials.^{8 9}

Although there have been new candidates targeting novel pathophysiological concepts, many have had disappointing results along the path of controlled trials.^{10 11} Opposite experience has occurred in drug development in rheumatoid arthritis: most drugs reaching the primary endpoint in phase II have also passed phase III. With this background, the results of clinical trials in SLE are even more disappointing, and the possible reasons and potential alternative post-hoc analyses are extensive.

With the aim of stimulating new developments in SLE trial design, an ‘Open Space’ discussion was performed on occasion of the European Lupus Meeting 2018 in Duesseldorf, Germany, about ‘What are the topics you care about for making trials in lupus more effective?’. The results are described in this report.

Principles of Open Space

Looking for a meeting technique that stimulates active contribution of every participants and allows discussion of all important topics present in the group, Open Space seemed most appropriate. Open Space is a self-organised process that practices inner discipline and collective activity and is thought to release the inherent creativity and leadership in people. By inviting participants to take responsibility for what they care about, Open Space intends to establish a marketplace of inquiry, reflection and learning, designed to bring out the best in both individuals and the whole.¹² Open Space is a specific method for conferences developed by Owen, which today is mostly used in change management, which describes a structured approach for organisational changes.¹³ It has been used for clinical conferences before.¹⁴

We used the Open Space technology for discussion of SLE trials, since the complexity of the disease and its treatment requires many stakeholders for a broad input and we were seeking an open, participant-driven discussion. Therefore, experts in lupus with great experiences in trials were invited and patients' representatives. As the basic intention was free scientific focused discussion rounds, other groups involved in drug development as government drug approval agencies and pharmaceutical industries were not invited.

Speakers of the European Lupus Meeting 2018 were invited to the Open Space meeting in English language with the topic 'What are the topics you care about for making trials in lupus more effective?'. Twenty-five experts (lupus experts, trial methodologists and a vasculitis trial expert), two patient representatives of Lupus Europe (the European joint organisation of regional lupus patient groups) and three local physicians joined the meeting, which was moderated by MS who had received a special training for Open Space management and organisation. It was the first Open Space experience for all participants.

As Open Space is a self-organising process and mainly participant-driven. All participants, who had equal rights, developed the meeting's agenda jointly by suggesting topics and voting for the preferred ones to discuss further. As a basic principle for Open Space, hierarchical structures are banned, and all opinions are of equal worth. The rules are simple: most important, there is the Law of Two Feet, which means every participant takes responsibility for what she/he cares about, stands up for that and uses his/her own two feet to move to whatever place he/she can best contribute and learn. Further, four principles apply to how to navigate in Open Space: *Whoever comes is the right people*, meaning that whoever is attracted to the same conversation are the people who can contribute most to that conversation—because they care; *Whatever happens is the only thing that could have*; *When it starts is the right time*; and *When it's over, it's over*.¹³ Scheduled time for this Open Space gathering was 1.5 days, in which four rounds were performed, with three levels of discussions each.

Table 1 Discussion topics identified as relevant to discuss in the first, second and third discussion round

	Topics first round	Votes (n)	Second/ third round
First session	Glucocorticoids	18	+
	Outcomes	16	+
	Stratification	16	+
	Basket trial	12	+
	Drug stop	10	
	Biomarkers/ biologically selected*	9	
Second session	Recruitment	11	+
	Placebo response	11	+
	Worth difference	6	
	Efficacy/effectiveness	4	
	Oncology/early disease	†	
	(Activity measures)†		

*Biomarkers and biologically selected patients were two different topics that were fused by the participants.

†No participant (law of two feet).

The meeting was sponsored by multipurpose arthritis centre 'Rheumazentrum Rhein-Ruhr', a non-profit association.

Discussion rounds

After introductions and an explanation of the Open Space concept and rules, the participants identified 13 topics which were they believed relevant for making lupus trials more effective (table 1). Each issue had been described by their proponent and similar or related ideas were merged, for example 'biomarkers' and 'biologically selected patients' were combined for further discussion. The first discussion level took place in two consecutive rounds with six topics each. Every discussion was structured by two to three guiding standardised questions (box 1); the content of the exchange in every group was open solely developed by the participating experts. All discussion processes and results were documented on flip charts. After the 12 discussion rounds of 120 min each, the results were presented to the whole group and further discussed in plenum. Public voting was done as part of the Open Space process to select areas for a second and third discussion and 6 of 12 topics were chosen. In contrast to the first open discussion round, rounds 2 and 3 were directed to focus on 'challenges' and 'needs for translation into practice', respectively. In the following we present the results of each discussion round, with the most important aspects visualised in figure 1. Importantly, brainstorming new ideas can be inhibited if people feel inhibited or defensive about their suggestion and providing evidence or details or even a formal rationale was discouraged from

Box 1 Specific questions addressed in each discussion round**Guiding question:**

'What are the topics you care about making trials in lupus more effective?'

Discussion rounds:

First

- ▶ What aspects have been discussed with regards to our topic and why?
- ▶ What are our main results?
- ▶ Which open issues/challenges do we face?

Second

- ▶ Identify urgent needs and their rationale.
- ▶ Which open issues/challenges do we face?

Third

- ▶ What is needed for the successful implementation of the identified urgent needs?
- ▶ What could be the next steps and who should be addressed?
- ▶ Which open issues/challenges do we face?

the beginning. Hence, we refrain from literature quotations in the Results section and present eminence-based opinions and facts.

Glucocorticoids—how to reduce oral steroids?

As in many other lupus meetings, the use of glucocorticoids (GC) in trials was selected as an important topic of discussion, due to their significant impact on outcomes and the need to avoid the harm associated with their use. In the first round, the aspects 'need for maintenance therapy', 'what is the safe dose—if there is one?', 'how to treat flares—with pulse or oral dose?' and 'tapering schemes' were identified as most important. As a result of the discussion, three study designs were developed: (1) A controlled withdrawal trial of GC with standardised documentation of clinical signs, symptoms and patient-reported outcomes (PRO); bio-specimens should be taken at several time-points to

identify predictors of flares posthoc. (2) A randomised controlled trial (RCT) to evaluate short term pulse vs oral dose GC with the outcomes *Definition of Disease Remission* (DORIS) remission,¹⁵ *Lupus Low Disease Activity State* (LLDAS)¹⁶ and PROs. (3) Trial to compare a fixed GC tapering protocol to GC reduction according to the treating physicians' discretion.

At the end of the first discussion round, agreement on standardised GC doses for pulses and tapering protocols as well as the definition of a right starting point for both tapering and GC withdrawal were still pending and seen by the group as challenges.

In the subsequent discussion rounds on GC, the need of optimising GC use was reaffirmed and the solutions to 'how to treat flares', 'pulse vs oral therapy', 'optimal dose' and 'lowest GC dose' were identified as crucial. Furthermore, in search of the ideal outcome for trials on GC, 'time to flare' and 'cumulative GC dosage' were chosen.

As the most important next step, the group recommended an ambitious GC protocol to treat flares and/or disease activity with no or only minimal damage and good quality of life (QoL) as the result. To design this trial, a literature search on GC use (pulses or oral) to treat flares was recommended and GC doses in patients in RCTs and in daily care should be analysed. Therefore, surveys on clinical practice should be performed or retrieved from existing data. Based on these data, an expert consensus trial protocol should be developed.

Finally, low flexibility of healthcare providers and authorities in changing the paradigm in GC use was seen as the most important unsolved issue in clinical trials. The challenge will be to find the balance between conclusions drawn from data, physicians' and patients' viewpoints and disease variability.

Outcomes

Organ specific manifestations, remission and LLDAS, PROs, new measures and especially challenges around the

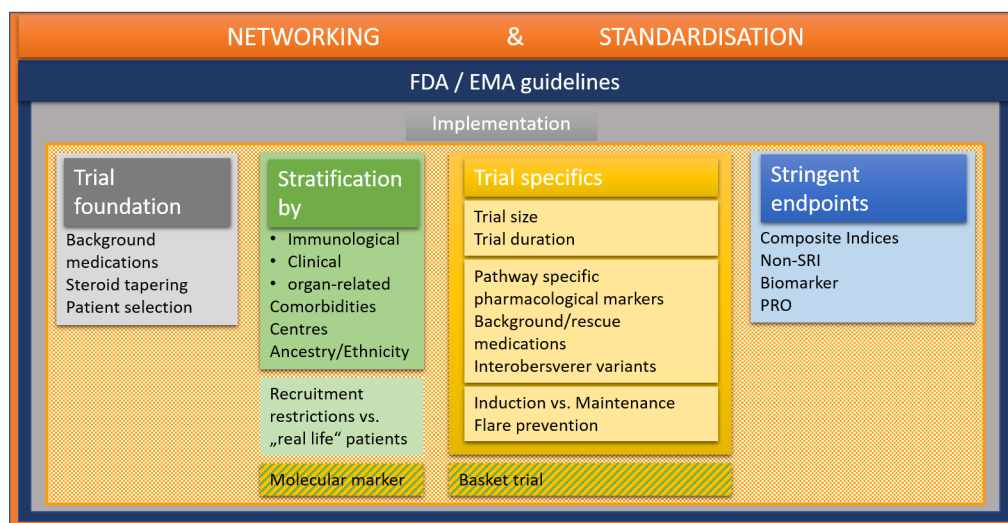


Figure 1 Aspects and contexts identified as relevant in SLE trials. PRO, patient-reported outcomes; SLE, systemic lupus erythematosus.

existing trial endpoint, SRI, were extensively discussed. Joint counts (tender and swollen), EULAR/ACR response definitions for lupus nephritis (excluding red blood count in urinary sediments) and Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) as a skin score were supported as possible organ specific outcomes. For non-organ specific outcomes like global disease activity or fatigue, the participants expressed the need for a new outcome variable. Remission, as it is defined by DORIS criteria, was felt to be better applicable for long-term studies, not as a primary outcome in RCTs. LLDAS was considered suitable for RCTs, although for some individuals, low disease activity may not be sufficient. Regarding SRI, the experts saw limitations mainly due to the SLE Disease Activity Index's (SLEDAI) insensitivity to change and the imbalance of response due to different SLEDAI domain weights. A combination of the SLE responder index 4 (SRI-4) with GC tapering was discussed as a potential composite measure. Such an approach would require standardising GC tapering, as the true challenge lies in different attitudes to reducing GC.

Based on the above stated limitations for commonly used outcome measures, the group identified an urgent need for new trial outcome(s). As a first modification, the change from measuring outcomes at a single time point to reaching a stable outcome over a certain period of time, ideally over the last period of a trial, was recommended. Regarding the type of measure, a continuous measure was preferred, which should take into account different grades of disease activity in each organ, such as the DAS-28 does in rheumatoid arthritis. The new activity index for trial outcome should summarise single-point organ specific complete or partial improvements with persistent response. For the implementation of a continuous activity index, defining thresholds of remission and LLDAS was seen as an option. The currently defined DORIS remission and LLDAS criteria were considered unsuitable for the 'usual' 52 weeks trials. PROs should be included into the outcome measure and GC should be reduced to unmask drug efficacy. The majority of the group believed that the ideal outcome should include physician and patient global assessment as well as low GC dosage.

Outcome instruments that meet the mentioned criteria should be validated in cohort studies as well as by applying them to datasets from clinical trials, particularly failed RCTs, and should then be tested in clinical care. The experts recommended that the validation should be a network approach, for example, by SLEuro, with the inclusion of recommendations for outcomes by a EULAR taskforce. The results will need to be discussed with drug licensing agencies (FDA and EMA) in order to be included into RCTs for new drugs.

At the end of the discussion, open issues for further discussion were a remission based on tissue samples (proof-of-concept trial), modifications of immunological

pathways and other outcomes that might allow a smaller number of patients for evaluation.

Patient/disease subsets—patient stratification

The heterogeneity of disease expression in SLE is generally seen as a major challenge for all trials. Classification criteria were developed as the first step to recruit a more homogenous population. The group discussed and recommended exploring alternative stratification methods like lupus nephritis versus non-renal SLE, based on single organ involvement or on disease patterns (eg, according to flares), on biomarkers (eg, conventional or interferon (IFN) signature), on baseline or historic characteristics, or on comorbidities and disease manifestations. Stratification should also consider background therapy.

To bring together all these aspects of stratification, the challenge will be to design several studies within the framework of one big trial. New, valid and reliable biomarkers would be a prerequisite for improved stratification methods. In such a master protocol, in addition to the conventional stratification to renal or extrarenal lupus, extended lupus nephritis strata categories could include new disease manifestation versus lupus nephritis flare versus refractory lupus nephritis, renal chronicity, ethnicity and potentially move away from the focus on just Class III and IV nephritis. Stratification of extrarenal lupus should be domain-specific. For example, there should be a differentiation between acute, subacute and discoid lupus skin manifestations and non-erosive, erosive and Jaccoud's arthropathy for arthritis. Other relevant parameters might be overall disease activity, disease duration or geographical region. In addition, creative approaches might include molecular signatures and biomarkers based on pathophysiology.

At this point in the discussion, concerns were expressed that such novel designs would not fit into current conservative regulatory policies and that insufficient stratification was the real problem of the past trial failures. To further explore this issue, a query of study databases (both failed and successful) is necessary, in which single organ domain trials and single organ parts of other studies should be analysed. In addition, the proposed master protocol needs discussion with regulatory authorities and (commercial) sponsors. For a better acceptance of such a protocol, it would be helpful to declare the subtypes of lupus, for example, lupus nephritis, as an orphan disease to minimise the burden of trials. Probably, the term 'rare and complex disease' would be helpful as successfully used in the European Reference Networks (ERN). Furthermore, an expert consent on reclassification of more homogeneous subsets of lupus would be quite beneficial.

The still pending issue from this discussion was whether sponsors would be willing to invest the necessary budget to develop drugs for rare diseases or for life-threatening cases to facilitate the approval process.

Basket trial in SLE

In a basket trial design, patient eligibility is defined by a particular biomarker or molecular alteration, and a specific disease itself, for example, a specific tumour type, is not a primary inclusion criterion. In such studies, biological profiles, for example, C4 complement deficiency in systemic connective tissue diseases (CTDs), would be linked to response and non-response to a specific intervention. Basket trials have just begun in cancer therapy. In rheumatology, no such trial has been done. The group discussed the benefits of basket trials such as potentially smaller sample sizes, a shorter duration and to be more powerful than conventional trials, with the effect size driving the design. The pathway related to the targeted biomarker or molecular alteration offers a specific readout, which might even be specific for individual organs. Analyses during the trial would enable early detection of responses and drug resistance and facilitate prompt adaptation of treatment.

In lupus or CTDs in general, the first challenge to design a basket trial will be to identify a suitable target accessible for intervention and present in a group of patients. Further needs are stable and reproducible signature(s) across CTDs, innovative drugs that match the signature, common clinical criteria for entry across diseases and adapted response criteria (across diseases vs organ specific response vs holistic response). Finally, FDA/EMA would have to approve the design for a new indication in SLE; a design that would be unprecedented and highly challenging.

Discussions with oncologists, information scientists and clinicians could be a next step. In parallel, high quality proteomic and genomic data from CTDs should be screened for signatures and alterations that could serve as inclusion criterion in a basket trial. Drugs with proven pharmacodynamic effect on the specific molecular pathway need to be identified or even newly designed.

Recruitment

Recruitment has been a critical challenge in every SLE trial, in particular the pool of eligible patients is small and recruitment often slower than estimated.

In this discussion, led by experts and patients, how to improve recruitment and retention of eligible patients was the dominant focus. The patients' motivation to participate in a trial is mostly intrinsically driven by the hope to get a new treatment and better care and by the feeling of being a part of something bigger. Further discussed challenges were the patients' adherence to treatment and the burden of frequent assessments in trials combined with distance. Financial allowances for patients were also debated.

The discussants agreed on the need for a network approach in conducting trials. Instead of single site trials, studies practically require multiple sites with clinics, private practices and patient organisations that actively participate. Such a network could improve awareness of existing trials and increase the pool of eligible participants

due to 'patient sharing'. Ideally, the patients would be entered into a registry and their information would be accessible for study personnel.

The networks could organise information campaigns on ongoing trials and help to create a positive perception of trials, in order to increase willingness to participate. Furthermore, general education of patients on adherence and their responsibilities and duties in clinical trials were stressed. These would hopefully reduce patients' concerns and eliminate fears of participating. In addition, less negative perception of trials could also reduce the placebo/nocebo responses since expectations might be less strong. All participants in the group (lupus experts and patients) demanded that patients be part of the trial team and not seen only as a test subject. Words of gratitude and information about trial results would be highly appreciated, and the consensus of the discussion was that these should be distributed after trial completion.

Further, the group agreed on a change of perspective: Instead of bringing patients into trials, the trials should be brought to the patients. Assessment at the patient's home or at least within short distance of home at a network site would reduce the burden of trials. Modern communication technologies will hopefully soon facilitate offering such options.

Major concerns regarding network trials were raised with a particular focus on legal obligations and the fear of opposition to the sharing of data. In addition, funding would have to be rearranged and clarified.

As next steps on the way to improve patient recruitment, the discussants agreed on the need of raising awareness, promoting the concept, content and necessary funding at pharmacological and state agencies and establishing a registry (eg, European-wide) with adequate partners (eg, ERN, SLEuro). Patients need to be integrated in all steps and should be supported to play an active role as a partner within the network.

Reduce the placebo response rate (entry criteria)

The observed placebo (PBO) responses in SLE are as much as twice those of trials of rheumatoid arthritis and psoriatic arthritis. Interestingly, PBO response seems to be lower in extrarenal trials than in lupus nephritis studies. A high PBO response lowers the effect size and ceiling effects are predicted. Recommendations from the group on reducing PBO rates were quite clear:

- ▶ exclude patients without classified SLE,
- ▶ omit 'soft' SLEDAI items, for example, alopecia, ulcers and inflated SLEDAI scores (elevated due to unspecific symptoms such as headache, arthralgia),
- ▶ omit items difficult to improve with therapy (eg, blood alterations such as white blood cell and platelet count),
- ▶ document findings for example, by photographs of skin findings or sonography for joints,
- ▶ add biomarkers as inclusion criteria, such as autoantibody titres, low complement, IFN-signature,

- ▶ move to domain specific measurements, for example, CLASI or joint counts,
- ▶ omit centre of high placebo response,
- ▶ measure drug levels during screening to exclude non-compliant patients,
- ▶ optimise background therapy,
- ▶ stop all background medications after 3 months as an optional concept

Without a doubt, these suggestions pose several challenges: Recruitment is becoming more difficult with stricter entry criteria, optimisation or stopping of background therapy will raise ethical issues and might result in lower recruitment and response rates, and marketing concerns by sponsors due to drug approval only for SLE subgroups might hinder drug development.

Designing trials with a drug stop phase

The topic of trials design with a ‘drug stopping phase’ overlapped with other discussion rounds and focused mainly on the improvement and new development of trial designs to reduce costs and improve efficiency. A drug stop design could be an option for non-severe cases in the maintenance phase of an early disease; probably most important these patients should be homogenous in disease expression. In addition, simpler measures and outcomes could facilitate such trials that otherwise should be performed in centres with expertise.

Biomarkers; selection of biologically selected patients for targeted therapies

Despite being addressed in several of the other rounds, there was an extra discussion on biomarkers only, emphasising their great perceived importance regardless of previous disappointing results. The potential relevance of biomarkers for improving diagnostics, predicting flares and changes in disease activity and monitoring, confirming or predicting treatment responses was discussed. For now, IFN-signature, histological findings, CD19+ B cell counts, antibodies (eg, anti-dsDNA, anti-C1q, anti-phospholipid antibodies) and complement deficiencies were named as classical candidates. It was stated that to date, no reliable biomarkers found general applicability, with urine biomarkers being the most promising candidates. Since no patient is like another, it was highly recommended to evaluate synergistic markers or sets of biomarkers and their predictive value regarding therapeutic response longitudinally.

Finding the difference that is relevant for patients or caregivers

This specific discussion on outcomes was mostly driven by the perceived vagueness of the connection between currently used trial endpoint and patient outcomes. It was agreed that patients should be included in trial development from the beginning and that their expectations regarding a successful trial outcome should be implemented in the design. An option could be the general inclusion of PROs as outcome parameters to capture the

patient-centred (vs clinician-measured) part of the treatment response (‘how are you’). In addition, the severity of (severe) adverse events should be indicated by the patients.

How to bridge the efficacy-effectiveness-gap?

Efficacy refers to the true biological effects of a drug, that is, addressing the question whether and how it actually works in a patient. Usually, the efficacy of a new drug is studied in clinical trials. In contrast to efficacy, effectiveness describes the extent to which a drug achieves its intended effect in the real-world clinical setting, that is, improvement in health in everyday practice. The improvements of patients’ outcomes achieved in clinical trials (efficacy) are often higher than those in everyday routine care (effectiveness). This led to the coining of the term ‘efficacy-effectiveness-gap’. During the Open Space gathering, the discussants developed ideas on how to measure effectiveness. Suggestions were conducting pragmatic trials, using claims data or running and analysing lupus registries. Relevant outcomes include quality of life, for example, Lupus Quality of Life questionnaire (LupusQoL) and measures for disease activity. Discussants emphasised the discordance of PROs and disease activity and it was generally questioned whether effectiveness was a good concept in all situations. The answer to that remains open for further discussions.

Oncology type trials in early cases

This discussion round aroused from a similar idea to the basket trial discussion. New designs, cost reductions and improved efficacy are urgently needed in lupus trials. Patients with early disease as a well-defined target population should be included in trials adapted from oncology with the primary aim of GC sparing. Crossover and ‘stop and watch’ designs were discussed as well as an ‘aggressive’ induction for these patients, for example, an anti-B cell therapy. Challenges of such trials will be to define the target population, to perform trials for single organ manifestations and the scant information that is available regarding the consequences of stopping treatment in lupus.

Activity measurement

The discussion round on activity measures did not take place as no one participated. We assume that this topic was considered too extensive to be discussed in the time available. Nonetheless, the authors consider it highly important for clinical trials.

CONCLUDING REMARKS

Despite great success in decreasing the standard mortality rate of patients with SLE over the last few decades, the current plateau in mortality and the high burden of the disease indicate an urgent need for new therapeutic options and a better use of already available drugs.¹ In the last few years, many promising medications failed to pass the hurdles of phase II and III clinical trials, preventing

drug approval. Intensive discussions and explorations of trial failures are ongoing,^{12 17 18} and as a result, a few modifications in trial design were seen in recent phase II trials. The results of currently ongoing phase III trials will finally show whether these changes were efficient.

Our Open Space discussion raised some issues that the field has been discussing without good solutions for quite some time. The ideal GC dose, how to treat flares, tapering GC ('lowest dose') and the stopping of GC are on top of this list. The optimisation of other background medications should be included in this context. It was recommended that the GC dose should also be included as part of the primary outcome.

Although no expert was keen to join the discussion on 'activity measurements', which thus did not take place according to Open Space rules, this topic was addressed in many other discussion rounds. Evaluation of the efficacy of newly developed drugs on disease activity should exclude soft SLEDAI items like alopecia and ulcers as well as altered serological parameter that may not be related to disease activity. Several discussions were in favour of using organ-specific indications as primary outcomes in trials. In general, the definitions of organ involvement and organ-specific treatment response need to be better specified and carefully documented, for example, with ultrasound imaging and differentiation between the various types of joint involvements.

A set of biomarkers, at best monitoring the mode of action of the evaluated drug, should be included as an exploratory part of every trial. Biomarkers and molecular signatures form the basis for new trial designs such as basket trials, which open up another possibility to broaden the patient population of a trial. In a next step, interdisciplinary discussion rounds with oncologists, immunologists and other specialists as well as information scientists and clinicians are needed, as well as high quality proteomic and genomic data from CTDs. Further, drugs with proven pharmacodynamic effects on previously identified molecular pathways need to be identified or developed and tested.

Many of these ideas, proposals and hypotheses can be evaluated in a first step by using data from previous lupus trials. One major challenge will be to find a balance between the conclusions drawn from the data, the clinicians' and patients' point of view, and the disease.

In addition to these recommendations addressing trial design, we identified several pretrial issues and the context of clinical trials as highly relevant for successful lupus trials. Of these, networking was a major topic. It starts locally with networks combining different levels of care to aid patient recruitment and standardise care of patients with SLE outside trials. A continuous exchange within these networks based on guidelines and recommendations should also include empowered patients educated in research and development as partners. Local networks should join bigger networks based on standardised documentation, for example, in registries. Such a system will facilitate recruitment of patient populations

with a better documented disease expression and lead to a harmonisation of patients' therapy, which would potentially result in more standardised background medication in trials.

If such networks were established worldwide, differences between various geographical regions, such as in placebo responses, could be reduced. Variation in care could be reduced by decision support systems, benchmarking and most importantly by consensus processes for standardisation. Those could lead to a paradigm shift in GC use towards a more homogenous handling of GC in routine care, which will significantly impact GC use in trials.

Such networking—locally, nationwide or even worldwide—is obviously challenging and needs support from organisations that combine their efforts. Thinking ahead, it could be the basis for successful trials in lupus and for a lower disease burden. Both these outcomes serve the same purpose, which is to improve the lives of patients with lupus.

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