Oral Presentations

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Moving towards new criteria in SLE, Sjögren's and APS

OP0001 THE LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) DEFINITION DISCRIMINATES RESPONDERS IN A SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) TRIAL: POST-HOC ANALYSIS OF THE PHASE IIB MUSE TRIAL OF ANIFROLUMAB

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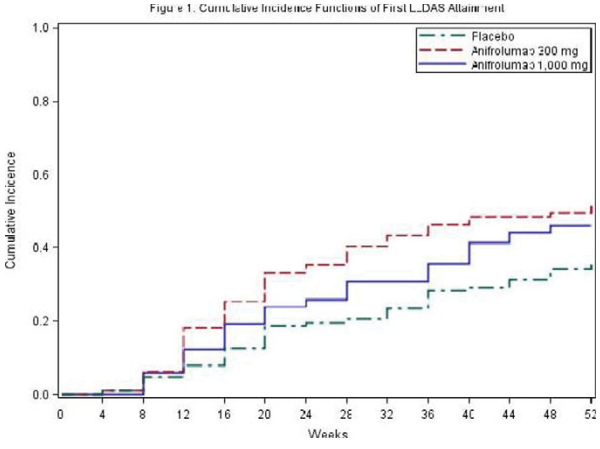
Background: A LLDAS definition has received preliminarily validation. Achieving low disease activity by this definition is associated with protection from damage accrual for patients (pts) with SLE.[1] However, it has not been evaluated as an endpoint in randomized controlled trials (RCTs).
Objectives: We evaluated LLDAS as an RCT endpoint in a *post-hoc* analysis of the MUSE trial of anifrolumab in pts with moderate to severe SLE.[2]
Methods: During the 52-week MUSE study, pts with active SLE received intravenous placebo, anifrolumab 300 mg, or 1,000 mg, in addition to standard of care, every 4 weeks for 48 weeks. LLDAS requires all of the following: SLEDAI–2K $\leq$4 without major organ activity, no new disease activity, PGA (0–3) $\leq$1, prednisolone $\leq$7.5 mg/day, and tolerance of standard immunosuppressant dosages.[1] LLDAS utility, its association with other endpoints, and discrimination between anifrolumab- and placebo-treated pts, were explored using descriptive statistics, logistic regression, and Gray's test. All randomized pts in MUSE were included in the analyses, and non-response imputation was performed after dropout.
Results: For pts receiving placebo (n=102), anifrolumab 300 mg (n=99), or anifrolumab 1,000 mg (n=104), LLDAS criteria were met at least once by 35%, 52%, and 46% of pts, respectively (odds ratio [OR] vs. placebo; 300 mg: 1.97, 95% CI 1.08, 3.58; p=0.027; 1,000 mg: 1.63, 95% CI 0.90, 2.95; p=0.103). Positive associations were observed between LLDAS and both the SLE Responder Index (SRI[4]) and BILAG-based Composite Lupus Assessment (BICLA), with 87% and 74% of pts attaining LLDAS at Week 52 also being SRI(4) and BICLA responders, respectively (χ^2=57.61 and 55.18; both $p<0.0001$). However, only 47% and 51% of SRI(4) and BICLA responders reached LLDAS. Increased LLDAS attainment from Week 12 (300 mg) or 28 (1,000 mg) was associated with anifrolumab treatment, compared with placebo (OR range; 300 mg: 1.7–3.6; 1,000 mg: 1.7–2.5). LLDAS was attained earlier (300 mg: χ^2=6.39, p=0.012; 1,000 mg: χ^2=2.44, p=0.119) in anifrolumab-treated pts (Figure 1). At Week 52, more anifrolumab-treated pts attained a LLDAS (OR vs. placebo; 300 mg: 3.41, 95% CI 1.73, 6.76, $p<0.001$; 1,000 mg: 2.03, 95% CI 1.01, 4.07, p=0.046). More anifrolumab-treated pts spent $\geq$50% of observed time in LLDAS (OR vs. placebo; 300 mg: 3.04, 95% CI 1.34, 6.92; p=0.008; 1,000 mg: 2.17, 95% CI 0.93, 5.03; p=0.072), and the OR of sustained LLDAS for at least six consecutive visits from Week 12 to 52 were 4.02 (95% CI 1.38, 11.73; p=0.011) (300 mg) and 2.95 (95% CI 0.99, 8.78; p=0.052) (1,000 mg).
Conclusions: LLDAS is associated with validated treatment response measures, SRI(4) and BICLA, but is more stringent than either. Anifrolumab was associated with $\leq$3.6-fold OR increases in LLDAS attainment, as well as greater aggregate and sustained time in LLDAS. This LLDAS definition should be considered as a study endpoint in SLE RCTs.



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[1] Franklyn K, et al. Ann Rheum Dis. 2015;75:1615–21.
[2] Furie R, et al. Arthritis Rheumatol. 2017;69:376–86.
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OP0002 MULTICRITERIA DECISION ANALYSIS FOR DEVELOPING NEW CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: EULAR and ACR are supporting multi-phase development of SLE classification criteria based on weighted criteria and a continuous probability scale. Prior steps included criteria generation, criteria reduction through Delphi and Nominal Group Technique exercises, literature review for sensitivity/specificity of candidate criteria, and organization of candidate criteria into seven clinical and three immunologic domains.
Objectives: To refine definitions of candidate criteria, determine relative weights using multicriteria decision analysis, and determine a threshold score for SLE classification.
Methods: An SLE Expert Panel (9 North American, 8 European) submitted 167 unique cases with a range of SLE probability. Experts scored 20 representative cases using the candidate criteria and rank-ordered them. In a 2-day meeting, experts reviewed inter-rater reliability of scoring, refined criteria definitions, and participated in a multicriteria decision analysis (MCDA) exercise using 1000Minds™ software. Experts were presented a series of decisions between two cases, each with different criteria from two domains (e.g. oral ulcers [cutaneous] and acute pericarditis [serositis] vs. alopecia [cutaneous] and pleural effusion [serositis]) and anonymously voted for the case more likely to be classified as SLE. Votes were discussed until consensus was reached for each decision. Using the consensus decisions, 1000Minds™ calculated criteria weights, assigned a total score to each of remaining 147 cases and rank-ordered the cases. Experts voted on whether each case should be classified as SLE. MCDA was repeated for criteria whose calculated weights were inconsistent with expert opinion until group consensus was achieved. 1000Minds™ then re-calculated criteria weights and re-ranked cases once. The score of the last case for which expert consensus was achieved was the threshold score.
Results: Inter-rater reliability was good; human data entry error, not following instructions, and differing interpretations of criteria definitions accounted for discrepancies. Arthritis and pericarditis definitions were modified through group discussion. The MCDA involved 74 pairwise decisions. Cranial neuropathy and Class VI lupus nephritis were removed as they added little to SLE classification. MCDA was repeated for the arthritis and cutaneous domains as initial weights did not match expert opinion. After criteria weights and scores were re-calculated once, experts reached consensus for SLE classification for case score $>$83.
Conclusions: Using an iterative process, the expert panel refined definitions, weighted candidate criteria and determined a threshold score of $>$83 for SLE classification, which will undergo validation.
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