

Abstract 97 Figure 1c Discriminant and ROC analysis which demonstrate the high specificity and sensitivity of dDOS when taking into account the rise time and the plateau time of the absorption signal (see Fig. 1b).

(eliminates inter-rater variability and operator dependency), low cost, and high speed of performance (~5 min per area of scanning) compared to US and MRI. dDOS has the potential to bring much-needed objectivity to the quantification of SLE arthritis.

Funding Source(s): N/A

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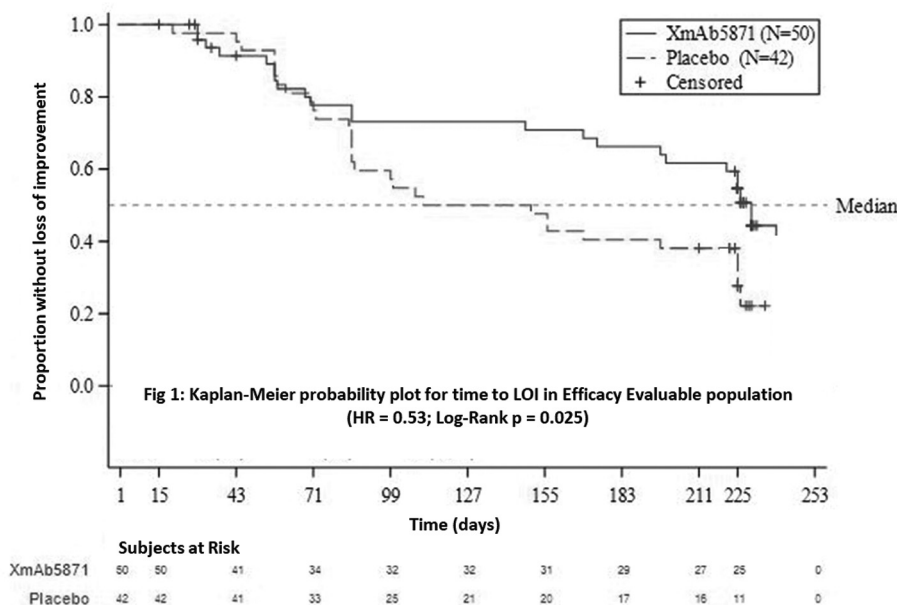
RESULTS OF A PHASE 2, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY OF A REVERSIBLE B CELL INHIBITOR, XMAB[®]5871, IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background XmAb5871 is a humanized anti-CD19 antibody Fc-engineered for increased affinity to FcγRIIb. Co-ligation of CD19 and FcγRIIb inhibits B lineage cells key to lupus pathogenesis. This Phase 2 study in SLE was designed to minimize background medications and placebo responses to improve interpretation of a small trial in a complex, heterogenous disease.

Methods Patients were enrolled with active, non-organ threatening disease, and treated until improved with 160 mg of IM Depo-Medrol. Immunosuppressive drugs were withdrawn except antimalarials or 10 mg/day prednisone or equivalent before randomization to IV XmAb5871 (5 mg/kg) or placebo. Study treatments were given Q14 days until Day 225 or loss of improvement (LOI), defined as SLEDAI increase 4 points OR new BILAG A or B, with investigator-rated clinical significance. At LOI, patients resumed standard of care. The primary endpoint was the proportion of subjects without LOI by Day 225 in the efficacy evaluable group (those who completed Day 225 or discontinued due to LOI or a drug-related adverse event). Patients who withdrew for other reasons were excluded from this analysis.



Abstract 98 Figure 1 Kaplan-Meier Probability Plot for Time to LOI in Efficacy Evaluable Population

Results 104 patients were randomized. In the efficacy evaluable population, 42% of XmAb5871-treated subjects reached Day 225 without LOI vs 28.6% of the placebo group ($p=0.18$) with 40.4% vs 23.1% ($p=0.06$) achieving this endpoint in the ITT population. In those with LOI, no (0%) XmAb5871 patients vs 9 (30%) placebo had SLE-DAI increase 7 with 3 (13%) vs 7 (23%) developing BILAG A scores. Six XmAb5871-treated patients were withdrawn for infusion-related events. The efficacy evaluable population excluded 10 placebo patients vs 2 XmAb5871 for other reasons, increasing placebo response proportions compared to the ITT population. Time to LOI was significantly longer in XmAb5871-treated patients than placebo ($p=0.025$, see figure 1).

The most common AEs in XmAb5871-treated patients were transient, infusion-related gastrointestinal side effects during the 1st or 2nd infusion. There were 8 SAEs in 7 XmAb-treated subjects, 5 in 4 placebo patients, no opportunistic infections, and no deaths. Infection rate was low compared to other SLE trials.

Conclusions Results from this small trial, designed to maximize interpretability, supports further evaluation of XmAb5871 in SLE.

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SENSITIVITY OF AN AUTOMATED FLUORESCENCE ENZYME IMMUNOASSAY VERSUS IMMUNOFLUORESCENCE AMONGST PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Background Antinuclear antibodies (ANA) play an important role in the diagnosis and classification of Systemic Lupus Erythematosus (SLE). Positivity of ANA by immunofluorescence (IIF) or an equivalent assay is part of the 1997 American College of Rheumatology (ACR) revised classification criteria and the 2012 revised criteria for the diagnosis of SLE from the Systemic Lupus International Collaborating Clinics (SLICC).

The aim of this study was to provide an overview of the sensitivity of automated fluorescence immunoassay (FEIA) versus IIF in SLE patients and consequently the number of false negatives.

Methods MEDLINE, EMBASE and Cochrane database searches (2000-March 2018) were conducted to identify fully-paired, cross-sectional or case-control studies of the diagnostic accuracy of FEIA and IIF in connective tissue diseases.

A meta-analysis of the sensitivity of FEIA versus IIF in SLE patients was conducted using hierarchical, mixed-effect models.

Methodological quality of included studies was assessed using the QUADAS-2 tool.

Results Out of 1798 papers identified, 11 studies (691 SLE patients) met the criteria for inclusion and reported the diagnostic accuracy of both IIF and FEIA. Four of the studies included consecutive patients (single-gate) and seven studies were case-control (two-gate).

Overall, sensitivity was 81% (95% CI 74%–86%) for FEIA and 88% (95% CI 79%–93%) for IIF, the difference being not statistically significant ($p=0.14$).

In the QUADAS-2 assessment, four studies included a positive ANA test as criteria for the diagnosis/classification of SLE which could introduce a high risk of bias in the overall sensitivity estimate. After excluding these four studies, the sensitivity point estimate for the remaining eight studies (431 patients) was 82% for FEIA and 81% for IIF ($p=0.9$).

Based on a 1.51% average prevalence of SLE in the single-gate studies, for every 1000 consecutive suspected patients screened, 15 patients will have SLE. Three out of fifteen will have a false negative test with FEIA versus two out of fifteen with IIF when sensitivity estimates from all studies are used. Three out of fifteen will have a false negative test with both tests when sensitivity estimates exclude the four studies that incorporated ANA results into the patient classification/diagnosis.

Conclusions Pooled sensitivity estimates of IIF and the automated FEIA in SLE patients was similar and not statistically different.

Taking into consideration the average prevalence of SLE in the single gate studies, both tests showed similar number of false negatives.

Funding Source(s): Carmen Andalucia and Sigrid Sjölander are Thermo Fisher Scientific employees. Michelle Orme was a Thermo Fisher Scientific consultant.

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DIFFERING OPINIONS ON CLINICAL RESEARCH BETWEEN HEALTHCARE PROVIDERS AND LUPUS PATIENTS

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Background Although systemic lupus erythematosus (SLE) disproportionately affects minority racial groups, they are significantly under-represented in clinical trials. This produces underpowered conclusions in race-based sub-group analyses. The decision to participate in clinical research is complex. Primary care providers (PCPs) have the ability to introduce the idea of clinical trials and to refer to specialists who participate in clinical trials. We evaluated SLE knowledge and implicit bias in clinical research participation in both PCPs and lupus patients.

Methods Lupus patients and PCPs completed a pre-test consisting of knowledge and belief questions followed by an educational program about lupus, clinical research, and human subjects protections. The same questions were repeated as part of the post-test. Responses to knowledge questions were analyzed by Fishers exact test for between group (patients vs. PCPs) comparisons or McNemars test for within group (pre-test vs. post-test) comparisons. Belief questions were scored on a Likert scale and analyzed by Mann-Whitney or Wilcoxon matched pairs for between group and within group comparisons.