analysis, the following were all associated with serious infection ($p<0.01$): splenectomy, use of cyclophosphamide, mycophenolate and rituximab, which is shown in figure 1 and figure 2.

Conclusions In the largest observational European Registry of SLE patients, one third of the jSLE patients suffered serious infections. Higher SLEDAI score, renal involvement and immunosupressant and corticosteroids use were independent associated factors to the presence of serious infection in jSLE, as well as smoking.

Funding Source(s): FIS Grant PI11/02857 (Instituto Carlos III, Fondos FEDER) has supported this work.

182 IMMODULATORY MEDICATION USE FOR YOUTH WITH NEWLY-DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2019-lsm.182

Background To examine immunomodulatory medication use for youth with systemic lupus erythematosus (SLE) during their first year of care.

Methods We conducted a retrospective cohort study using de-identified administrative claims for 2000 to 2013 from Optum© Clinformatics® DataMart for youth ages 10–24 years with an incident diagnosis of SLE (3 International Classication of Diseases, Ninth Revision codes for SLE 710.0, each >30 days apart). We determined the proportion of subjects filling a prescription for an immunomodulatory mediation, defined as hydroxychloroquine or an immunosuppressant (excluding glucocorticoids), within 3, 6, and 12 months after the first SLE diagnosis code (index date). We used a Cox proportional hazards regression model to examine associations between time to immunomodulatory prescription fill within 12 months and demographic and disease factors (age, race/ethnicity, household education level, region, history of seizures/stroke, history nephritis).

Results We identified 650 youth with an incident diagnosis of SLE. In the 12 months following the index date, 511 (79%) of youth had a prescription fill for an immunomodulatory medication. For those with a prescription fill for hydroxychloroquine in the first year (n=457, 70%), 374 (58%) and 407 (63%) of youth filled the medication within 3 months and 6 months from the index date, respectively (table). For those with a prescription fill for an immunosuppressant (n=221, 34%) in the first year, 114 (18%) and 162 (25%) of youth filled the medication within 3 months and 6 months from the index date, respectively (Table). Location in the Northeast region was significantly associated with a longer time to immunomodulatory prescription fill within 12 months, compared to location in the South (HR=0.686, 95% CI 0.50–0.94). There were no statistically significant associations for the other demographic and disease factors.

Abstract 182 Table 1 Immunomodulatory Medication Use in Youth with Newly-Diagnosed SLE, N=650

Proportion with prescription fills after first SLE diagnosis code, n (%)	Within 3 months	Within 6 months	Within 1 year
Immunomodulatory medication (hydroxychloroquine or immunosuppressant)	428 (66)	460 (71)	511 (78)
Hydroxychloroquine	374 (58)	407 (63)	457 (70)
Immunosuppressant	114 (18)	162 (25)	221 (34)

Immunosuppressant medications include: mycophenolate mofetil, azathioprine, leflunomide, methotrexate, tacrolimus, and oral cyclophosphamide.

Conclusions Among youth with newly-diagnosed SLE, hydroxychloroquine use is prevalent although not universal, and immunosuppressant use is notably low during the first year of care. As poorly controlled SLE disease activity can lead to organ damage, further work is needed to identify potential factors contributing to suboptimal immunomodulatory medication use in this population.

Funding Source(s): The Childhood Arthritis and Rheumatology Research Alliance, Alpha Omicron Pi Foundation

183 A PHASE 1B/2A TRIAL OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN SYSTEMIC LUPUS ERYTHEMATOSUS

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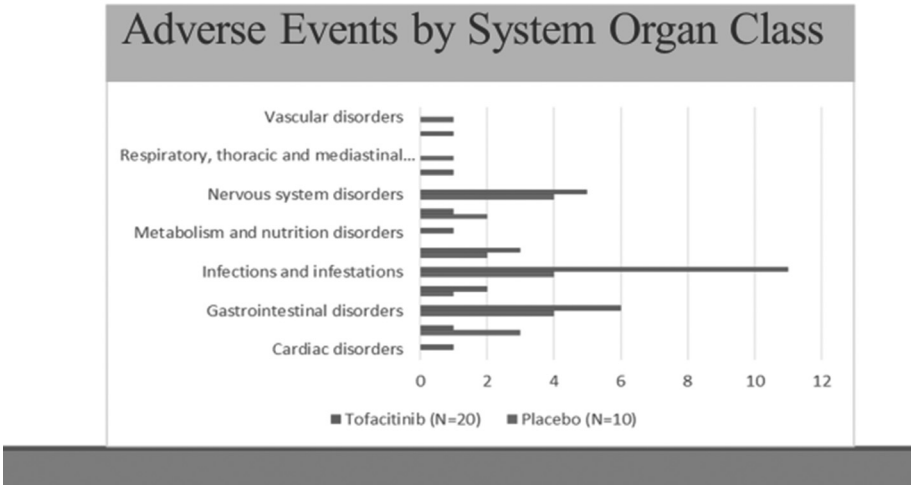
10.1136/lupus-2019-lsm.183

Background A pharmacologic intervention that modulates JAK/STAT signaling pathways represents a novel approach for the treatment of Systemic Lupus Erythematosus (SLE). In animal models of SLE, tofacitinib improved clinical features, immune dysregulation and vascular dysfunction. The STAT4 risk allele is associated with higher risk of severe manifestations in SLE. We hypothesized that immune modulation in response to JAK/STAT inhibition would be more robust in SLE subjects that carry the STAT4 risk allele.

Methods We conducted a phase 1b/2a randomized, double-blind, placebo-controlled clinical trial of oral tofacitinib, 5 mg twice daily, in 30 SLE subjects (2:1 drug to placebo ratio) with mild to moderate disease activity, stratified by the presence or absence of STAT4 risk allele. Study duration was 84 days (56 days of active treatment ; 28 days of off drug). In addition to recording adverse events (AEs), lipoprotein profile, non-invasive vascular function studies, immuno-phenotyping, and gene expression studies were performed.



Abstract 183 Figure 1 Adverse Events by Organ System. Adverse Events in Subjects on Tofacitinib vs Placebo

Results Tofacitinib was well tolerated with no worsening of SLE disease activity, and no severe AEs, opportunistic infections or liver function abnormalities. A total of 43 AEs (mostly mild respiratory infections) occurred in the treated group compared to 28 AEs in placebo. There was a significant increase in HDL-C and HDL particle size in tofacitinib-treated patients at day 56 (p=0.006) accompanied by significant improvements in plasma protein lecithin: cholesterol acyltransferase (LCAT) concentration. There were also trends for improvements in vascular stiffness in the tofacitinib-treated group. The Interferon response genes (type I IFN), the levels of low- density granulocytes (LDGs) and neutrophil extracellular trap (NET remnants) significantly decreased in the tofacitinib treated group who were STAT 4 risk allele positive but not in the placebo group at day 56, accompanied by significant changes in pSTAT phosphorylation of different immune cells. Levels of activation and checkpoint markers CD103, CXCR3, ICOS, and PD-1 were significantly decreased on multiple T cell subsets, in tofacitinib treated individuals that lack the STAT4 risk allele.

Conclusions In a short-term trial, tofacitinib was well tolerated in SLE subjects with mild-moderate disease activity. Use of tofacitinib resulted in improvements in lipoprotein profile and HDL function and decreases in the type I IFN and aberrant neutrophil responses characteristic of SLE. Long-term studies are needed to determine the efficacy of tofacitinib in the various manifestations of SLE.

Funding Source(s): Intramural Research Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health and in part by Pfizer Inc.

Adverse Events in Subjects on Tofacitinib vs Placebo

184 PATIENT PERCEPTION OF SLE BURDEN: THE ROLE OF DISEASE ACTIVITY, COMORBIDITIES AND TREATMENT

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10.1136/lupus-2019-lsm.184

Background Physician-based assessment of SLE activity and damage may not be able to capture the real disease impact on patients life. Objective of our study was to investigate the role of disease activity, comorbidities and treatment in determining patient perception of SLE burden.

Methods This is a cross-sectional study that enrolls patients with a diagnosis of SLE (ACR 1997 criteria). For each patient, demographics, comorbidities, treatment, clinical and laboratory data were collected. Disease activity was evaluated with the SELENA-SLEDAI score and organ damage with the SLICC/DI. The Lupus Impact Tracker (LIT) questionnaire was used to assess SLE impact. The Spearman test has been used for linear correlation between continuous data.

Results We included 195 adult SLE patients (97,4% Caucasian, 94,4% female, mean age 44,212,8 years, median disease duration 13 years).

Median SLEDAI at enrollment was 2 (IQR 0–4) and median SLICC/DI was 0 (IQR 0–2). 9,8% of patients had a concomitant fibromyalgia. The most frequent active disease manifestations at baseline were hematological (27/195), articular and cutaneous (24/195 both); 13 patients had active renal involvement. 52,8% of the cohort was on steroid therapy with a mean daily dose of 2,84,9 mg of methylprednisolone. 46,15% was on immunosuppressive treatment and 77,95% on hydroxychloroquine (HCQ). The median LIT score was 20 (IQR 7,5–37,5).

Among the LIT items, those with the highest score, suggestive of a severe disease impact, were: anxiety, fatigue and pain. We found no significant correlation between SLEDAI and the score of each LIT item.

We found that active articular and cutaneous manifestations, but not renal involvement, influence patient subjective perception of SLE impact. In the multivariate analysis, active arthritis shows a significant correlation with LIT items relative to: pain (p=0,02), daily activities and future planning (p<0,01), irrespective of comorbidities. Fibromyalgia resulted associated with a higher score for the item of fatigue (p<0,01).

Finally, we found that also ongoing therapy can contribute to determine SLE burden. In the multivariate analysis, we found a significant correlation between steroid therapy and higher scores for the items of family responsibilities, future planning, discomfort due to physical appearance and drug side effects (p<0,01), irrespective of disease activity.