Abstract 289 Table 1

ACR/EULAR criteria	At EULAR/ACR classification, % n=558	EULAR/ACR met at the same time, % n=344	EULAR/ACR met earlier, % n=41	EULAR/ACR met later, % n=173	p value*
CLINICAL					
Oral ulcers	30.7	25.3	0.0	48.6	<0.0001
Discoid rash	9.7	8.1	0.0	15.0	0.0027
Malar rash	45.3	38.1	14.6	67.1	<0.0001
Arthritis	66.1	68.3	14.6	74.0	<0.0001
Psychosis	3.1	3.2	0.0	3.5	0.7848
Seizures	5.0	6.4	2.4	2.9	0.1821
Pleurisy	35.8	38.7	22.0	33.5	0.0817
Leukopenia	40.5	40.7	19.5	45.1	0.0093
Thrombocytopenia	12.9	14.2	12.2	10.4	0.4736
Autoimmune hemolysis	7.9	7.0	19.5	6.9	0.0307
Proteinuria	23.5	26.5	31.7	15.6	0.0080
Renal biopsy II or V	8.2	8.1	26.8	4.0	0.0001
Renal biopsy III or IV	4.7	4.1	9.8	4.6	0.2405
IMMUNOLOGIC					
aCL>40	16.9	15.4	12.2	20.8	0.2411
Anti-Smith	30.3	35.8	26.8	20.2	0.0010
Anti-dsDNA	52.1	58.4	53.7	39.3	0.0002

*By Chi square and Fisher's exact as appropriate

ACR/EULAR criteria	At EULAR/ACR classification, % n=956	EULAR/ACR met at the same time, % n=556	EULAR/ACR met earlier, % n=71	EULAR/ACR met later, % n=329	p value*
CLINICAL					
Fever	64.6	64.4	59.2	66.3	0.515
Oral ulcers	45.4	41.6	36.6	53.8	0.001
Alopecia	64.9	65.7	60.6	64.4	0.687
Subacute cutaneous lupus	4.3	5.0	2.8	3.3	0.397
Discoid lupus	11.2	10.6	1.4	14.3	0.006
Acute cutaneous	69.0	65.5	54.9	78.1	<0.0001
Synovitis	84.6	83.1	78.9	88.5	0.039
Psychosis	7.6	6.7	9.9	8.8	0.386
Seizures	10.3	10.1	8.5	10.9	0.802
Pleural or pericardial effusion	31.4	30.9	26.8	33.1	0.543
Pericarditis	16.6	16.6	16.9	16.7	0.996
Leucopenia	56.7	55.8	53.5	59.0	0.554
Thrombocytopenia	24.3	24.1	25.4	24.3	0.973
Autoimmune hemolysis	13.6	16.7	7.0	9.7	0.003
Proteinuria	48.3	47.5	50.7	49.2	0.807
Renal biopsy II or V	7.6	6.5	8.5	9.4	0.270
Renal biopsy III or IV	19.1	19.2	21.1	18.5	0.876
IMMUNOLOGIC					
aCL IgG >40 GPL or or anti-ß2 microglobulin>40 or LAC	38.7	38.0	39.4	39.8	0.852
C3 or C4	59.0	59.5	64.8	56.8	0.431
C3 and C4	44.4	46.2	46.5	40.7	0.263
Anti-Smith	26.3	26.4	22.5	26.8	0.756
Anti-dsDNA	67.6	68.7	77.5	63.5	0.051

*By Chi square

earlier had a lower frequency of milder manifestations (like mucocutaneous and articular) and tend to have a higher frequency of anti-dsDNA antibodies, suggesting these criteria could be more useful in subsets of patients with more severe disease.

Funding Source(s): None

290 DEVELOPMENT AND FIRST-IN-HUMAN CHARACTERIZATION OF AN ICOSL AND BAFF BISPECIFIC INHIBITOR AMG 570 FOR SLE TREATMENT

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10.1136/lupus-2019-lsm.290

Background Autoimmune diseases, including systemic lupus erythematosus (SLE), are associated with dysregulated T cell and B cell responses. AMG 570 is a bispecific molecule targeting T cell and B cell activity through inhibition of inducible costimulator ligand (ICOSL) and B cell activating factor (BAFF). We hypothesize that targeting both ICOSL and BAFF will be more effective than single target inhibition in SLE and other autoimmune diseases. We investigated if targeting ICOSL and BAFF has superior efficacy to single target inhibition in mouse arthritis and lupus models. We also investigated the safety, tolerability, pharmacokinetics, and pharmacodynamics of AMG 570 in healthy subjects after single subcutaneous doses.

Methods A murine surrogate ICOSL/BAFF bispecific along with single or combination inhibition was evaluated in the mouse collagen-induced arthritis (CIA) and NZB/NZW lupus

models. AMG 570 binding affinity to human and cyno ICOSL/BAFF was tested by Kinexa A. An ongoing, first-in-human study has enrolled healthy adult subjects into 6 escalating single-dose cohorts. Eight participants were enrolled into each cohort and randomized 3:1 to receive AMG 570 or placebo. The primary endpoint was treatment-emergent adverse events (AEs). Secondary endpoints included pharmacokinetics and pharmacodynamics.

Results ICOSL and BAFF dual inhibition was more effective than single inhibition in ameliorating arthritis incidence and severity in the mouse CIA model as well as reducing anti-dsDNA IgG, delaying proteinuria and improving survival in the NZB/NZW lupus model. Based on high affinity to ICOSL and BAFF, AMG 570 was selected for investigation in a single ascending dose study in healthy subjects. As of an ad hoc interim analysis following six cohorts, 48 healthy participants received one dose of investigational product (AMG 570 or placebo). Overall, 73 mild to moderate AEs were reported. The most common AEs were upper respiratory tract infection and injection site erythema. No drug-related serious AEs or fatal AEs were reported thus far. AMG 570 demonstrated nonlinear pharmacokinetics consistent with cell surface ICOSL binding. At the highest dose tested, AMG 570 achieved >90% mean ICOSL receptor occupancy on circulating B cells 8 days after dosing. AMG 570 led to a reduction in circulating naïve B cells and an increase in circulating memory B cells.

Conclusions Dual inhibition of ICOSL and BAFF is more efficacious than single target inhibition in mouse disease models. In healthy subjects to date, single doses of AMG 570 have been safe, well tolerated, and demonstrated pharmacodynamic activity consistent with inhibition of both ICOSL and BAFF.

Funding Source(s): Amgen Inc.

291 ASSESSMENT OF THE QRISK2, QRISK3, SLE CARDIOVASCULAR RISK EQUATION, MODIFIED FRAMINGHAM AND FRAMINGHAM RISK CALCULATORS AS PREDICTORS OF CARDIOVASCULAR DISEASE EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2019-lsm.291

Background Systemic lupus erythematosus (SLE) is recognised as an independent risk factor for cardiovascular disease (CVD). This study aimed to determine which cardiovascular risk assessment tool: QRISK2, QRISK3, Framingham (FRS), Modified FRS (mFRS) or SLE Cardiovascular Risk Equation (SLECRE) best predicts CVD in SLE. QRISK3, mFRS and SLECRE are CVD risk assessment instruments considering SLE in risk prognosticating patients.

Methods Single-centre analyses on prospectively collected data of 1887 SLE patients were performed to compute 10 year CVD risk scores for each tool. Tools scores were evaluated against CVD development at or within ten years for cases (CVD events) and controls (no CVD events). For cases, the index date for risk score calculation was chosen 10 years, or as close to 10 years as possible prior to the CVD event. Similarly, for controls, risk scores were calculated as close to 10 years as possible prior to the most recent clinic appointment. Proportions of patients classified as low risk (<10%), median risk (10%–20%) and high risk (>20%) of developing CVD according to each tool were determined. Sensitivity, specificity, positive/negative predictive values and c-statistics of these tools were analysed.

Results 232 total CVD events were seen in the cohort including myocardial infarction, stroke, transient ischemic attack, heart failure and CVD death. QRISK2 and FRS performances were similar, while the QRISK3 and mFRS performances were similar. The SLECRE classified the highest number of patients

Abstract 291 Table 1 Percentage of cases and controls classified as low (<10%), median (10–20%) and high risk of developing CVD according to each CVD risk assessment tool

Tool	CVD Status	Low Risk (<10%) (%)	Median Risk (10 – 20%) (%)	High Risk (>20%) (%)
QRISK2	Cases	81	14	4
	Controls	93	5	2
FRS	Cases	78	16	6
	Controls	93	6	1
QRISK3	Cases	53	27	20
	Controls	78	13	9
mFRS	Cases	54	25	21
	Controls	83	10	7
SLECRE	Cases	39	29	32
	Controls	64	23	13