MTX-IR pts with RA. However, clinical outcomes of all 3 regimens, including tofacitinib 5 mg BID monotherapy, were comparable. There were no new or unexpected safety issues.

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FRIDAY, 16 JUNE 2017

New treatments in SLE, Sjögren's and APS

OP0231 THE EFFECT OF "TRIPLE THERAPY" WITH ANTICOAGULATION PLUS CORTICOSTEROIDS PLUS PLASMA EXCHANGE AND/OR INTRAVENOUS IMMUNOGLOBULINS ON THE MORTALITY OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS) PATIENTS

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Background: Triple therapy (anticoagulation plus corticosteroids plus plasma exchange and/or intravenous immunoglobulins) is empirically prescribed for the management of catastrophic antiphospholipid syndrome (CAPS). However, previous analyses have been inconsistent regarding the beneficial effect of triple therapy on patients' survival.

Objectives: The objective of this study was to assess the effect that triple therapy has on the mortality risk of CAPS patients.

Methods: In a cohort including 525 episodes of CAPS (CAPS Registry), we evaluated the relationship between triple therapy and mortality. Patients were grouped in three based on their treatments: a) triple therapy (anticoagulation plus corticosteroids plus plasma exchange and/or intravenous immunoglobulins); b) drugs included in the triple therapy but in different combinations; c) none of the treatments included in the triple therapy. The primary endpoint was all-cause mortality. Multivariate logistic regression models were used to compare mortality risk between groups taking into account a set of possible confounding variables.

Results: The "CAPS registry" cohort included 525 episodes of CAPS accounting for 502 patients. After excluding 38 episodes (7.2%), a total of 487 episodes of CAPS accounting for 471 patients (mean age 38 years; 67.9% female; primary APS patients 68.8%) were analyzed. Overall, 177 (36.3%) patients died. Triple therapy was prescribed in 197 episodes (40.5%), other combinations in 278 (57.1%), and none of those treatments in 12 episodes (2.5%). According to these three groups, mortality rate increased up to 27.9%, 40.6%, and 75%, respectively. Triple therapy was positively associated with a higher chance of survival when compared to non-treatment (adjusted odds ratio [OR]: 7.7 95%; confidence interval [95CI] 2.0–29.7) or to treatment with other combinations of drugs included in the triple therapy (adjusted OR 6.8; 95CI 1.7–26.9). Triple therapy accounted for a 64% decrease of the risk of death in patients with CAPS that received this combination of drugs.

Conclusions: Triple therapy is independently associated to a higher survival rate among CAPS.

Acknowledgements: To the CAPS Registry Project Group (European Forum on Antiphospholipid Antibodies).

Disclosure of Interest: None declared

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OP0232 SUSTAINED SAFETY AND EFFICACY OVER 10 YEARS WITH BELIMUMAB (BEL) PLUS STANDARD SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) THERAPY (SOC) IN PATIENTS WITH SLE

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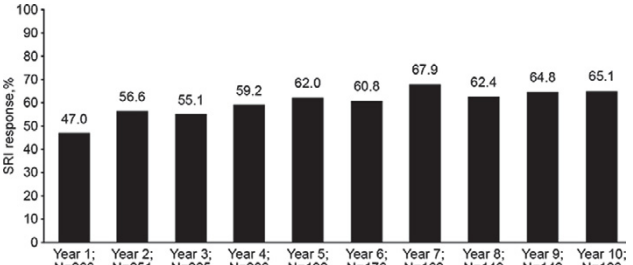
Background: Preliminary safety and efficacy data from the Phase II BEL open-label extension study (LBSL02; NCT00071487) have been reported.

Objectives: Here we present the final 10-year data.

Methods: This was a multicentre, open-label, continuation trial (BEL112626; NCT00583362) of BEL + SoC in patients with a satisfactory response in the parent study. Patients received intravenous BEL 10 mg/kg every 4 weeks. Baseline was prior to the first ever dose of BEL.

Results: Of 298 patients in the continuation trial, 131 (44%) remained at Year 10. Total BEL exposure was 2154 patient-years. Adverse events (AEs) remained stable or decreased (Table). Two deaths (pseudomonal lung infection; cytomegaloviral pneumonia) were possibly related to BEL. SLE Responder Index (SRI) response increased (Figure). A British Isles Lupus Assessment Group (BILAG) flare (1 new A/2 new B scores) occurred in 72.6% of patients and 41.9% had a severe flare (SLE Flare Index). Prednisone dose decreased from baseline to Year 10 (Table). Of patients receiving >7.5 mg/day baseline prednisone, 32.6%



Abstract OP0232 – Table 1

	0–1y (N=296)	1–2y (N=294)	2–3y (N=276)	3–4y (N=250)	4–5y (N=223)	5–6y (N=209)	6–7y (N=192)	7–8y (N=178)	8–9y (N=169)	9–10y (N=152)	10–11y (N=131)
Incidence of ≥1 AE, n (%)											
Overall	291 (98.3)	283 (96.3)	260 (94.2)	239 (95.6)	203 (91.0)	190 (90.9)	182 (94.8)	162 (91.0)	157 (92.9)	137 (90.1)	105 (80.2)
Resulting in discontinuation	2 (0.7)	3 (1.0)	3 (1.1)	7 (2.8)	5 (2.2)	6 (2.9)	6 (3.1)	1 (0.6)	3 (1.8)	5 (3.3)	2 (1.5)
Serious AE	41 (13.9)	43 (14.6)	50 (18.1)	30 (12.0)	40 (17.9)	33 (15.8)	35 (18.2)	34 (19.1)	28 (16.6)	25 (16.4)	14 (10.7)
Serious infections/infestations	11 (3.7)	13 (4.4)	9 (3.3)	9 (3.6)	6 (2.7)	6 (2.9)	12 (6.3)	10 (5.6)	8 (4.7)	5 (3.3)	5 (3.8)
Death	1 (0.3)	0	1 (0.4)	1 (0.4)	0	1 (0.5)	2 (1.0)	0	0	1 (0.7)	0
		Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
Prednisone											
median % change from baseline;		-0.4;	-25.0;	-36.9;	-50.0;	-48.3;	-60.0;	-62.5;	-70.0;	-66.7;	-65.8;
25th, 75th percentile (n)		-50.0, 0 (186)	-74.2, 0 (172)	-80.0, 0 (153)	100.0, 0 (140)	-100.0, 0 (128)	0 (115)	-100.0, -10.7 (105)	-100.0, -1.6 (94)	-100.0, -0 (91)	-100.0, 0 (84)

(14/43) decreased their dose to ≤7.5 mg/day by Year 10; 9.5% (9/95) of patients receiving baseline prednisone ≤7.5 mg/day had a dose increase to >7.5 mg/day.
Conclusions: Over 10 years BEL + SoC was well tolerated and the rates and nature of AEs were consistent with the known profile of BEL. Efficacy was maintained and prednisone use decreased in those receiving >7.5 mg/day at baseline.
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OP0233 PRIMARY PROPHYLAXIS OF CARDIOVASCULAR EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS OF 291 PATIENTS FROM TWO ITALIAN CENTERS

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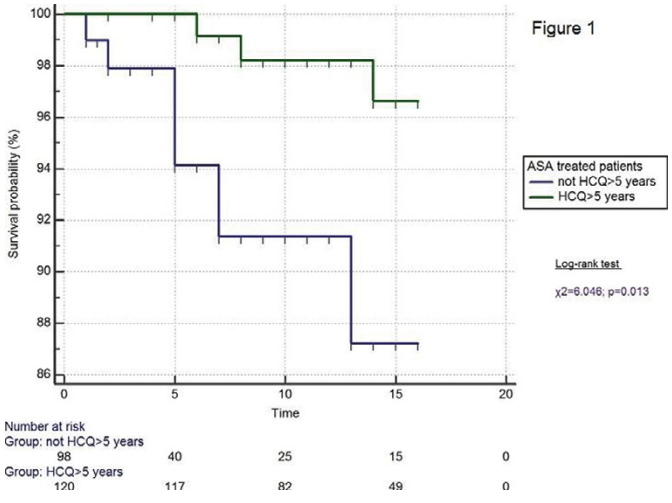
Background: Systemic lupus erythematosus (SLE) is associated with an increased cardiovascular (CV) risk (1). By retrospectively investigating a one centre cohort, we have recently reported that low-dose aspirin (ASA) use is associated with a reduced CV risk in SLE (2) and long-term hydroxychloroquine (HCQ) exposure may have an additive effect (3).
Objectives: This study was conducted on 2 Italian SLE cohorts to confirm these results and assess the role, if any, of statins.
Methods: Clinical charts of SLE patients consecutively admitted to 2 University Rheumatology Units from November 2000 to December 2014 who, at admission, had not experienced any CV event, were investigated. ASA, HCQ and statins use and the occurrence of any CV event, were recorded at each visit. Kaplan-Meier analysis was performed to determine the HCQ exposure status associated with a higher CV-free survival. Cox regression analysis was carried out to identify factors independently associated with a first CV event.
Results: A total of 291 SLE patients were included in the study and followed for a median of 8 years. During follow-up, 16 CV events occurred. Kaplan Meier analysis revealed a greater CV event-free rate in the 120 ASA-treated patients taking HCQ at standard dose for more than 5 years than in the 98 patients treated with ASA alone or with HCQ for less than 5 years (Figure 1). At univariate analysis, patients with a first CV event compared with those without any thrombotic events were antiphospholipid antibody (aPL) positive (P=0.017 HR 2.91) and had significantly higher blood pressure (P=0.017 HR 3.58), hypercholesterolemia (P=0,015 HR 3.40) and higher disease damage at last visit (P=0,032 HR 1.56). Moreover, ASA treatment (P=0,012 HR 0.27) and HCQ use (P=0,012 HR 0.26) for more than 5 years were negative predictors, while statins use did not show any association (P=0.619). All other variables examined, including smoking, obesity, hypertriglyceridaemia, diabetes mellitus, disease activity, severe SLE, other medications (immunosuppressive agents, steroids) were not associated, either positively or negatively, with the occurrence of CV events. At multivariate analysis, taking ASA and HCQ for more than 5 years were protective against thrombosis (HR 0.24 and HR 0.27, respectively), while aPL positivity (HR 4.32) increased the risk of a first CV event.



Conclusions: Use of antimalarials for more than 5 years is associated with a reduced risk of a first thrombosis in SLE patients and the HCQ-ASA combination seems to synergistically reduce further the CV risk. Larger, prospective studies are needed to provide a better definition of the role of these drugs in CV primary prevention in SLE.
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OP0234 CLINICAL AND BIOLOGIC EFFECTS OF ICOSL BLOCKADE BY AMG 557 IN SUBJECTS WITH LUPUS ARTHRITIS

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Background: Blockade of inducible costimulatory ligand (ICOSL) might be a promising approach for autoimmune diseases such as systemic lupus erythematosus (SLE). We evaluated AMG 557, an anti-ICOSL monoclonal antibody, in an exploratory phase 1b study of SLE subjects with inflammatory arthritis, by withdrawing background therapies to improve interpretability of a small study.
Objectives: To investigate potential efficacy, safety, and tolerability of AMG 557 in subjects with lupus arthritis.
Methods: This double-blind, randomized, placebo-controlled trial enrolled subjects with SLE and active lupus arthritis (≥4 tender and 4 swollen joints) and Systemic Lupus Erythematosus Disease Activity Index [SLEDAI] score ≥6 despite stable background immunosuppressants. Upon enrollment, investigators were permitted to use up to 20 mg/day of prednisone, which was tapered by day 85 to 7.5 mg/day or 50% of baseline, whichever was lower. Subjects received AMG 557 210 mg or placebo once weekly for 3 weeks followed by 10 additional doses every other week until day 155. At day 29, background immunosuppressants were withdrawn. The primary clinical endpoint was a composite Lupus Arthritis Responder Index at day 169; response was defined as achieving: (1) 50% decrease in combined tender and swollen joint counts, and (2) ≥1 letter improvement in the musculoskeletal subsystem of the British Isles Lupus Assessment Group (BILAG) index and (3) prespecified immunosuppressant medication withdrawal and/or prednisone taper. Safety was a co-primary endpoint. Exploratory endpoints included safety, 4-point reduction of SLEDAI, clinical indices (SLEDAI, BILAG), complement components, autoantibodies, and lymphocyte populations.
Results: Twenty subjects (19 females) were randomized (10 AMG 557, 10 placebo) at 8 sites in North America, Asia, and Europe. The primary endpoint was met by 3/10 subjects receiving AMG 557 and 1/10 subjects receiving placebo (*P*=ns). A 4-point decrease in SLEDAI score was achieved by 7/10 subjects on AMG 557 and 2/10 subjects on placebo. At day 169, subjects receiving AMG 557 had decreases from baseline in mean global BILAG and SLEDAI scores of 36% and 48% respectively, compared to 25% and 11% in subjects receiving placebo. Lupus-associated biomarkers, including serum complement indices (C3, C4, and CH50), and autoantibodies, including anti-dsDNA, demonstrated trends towards improvement relative to placebo. Treatment-emergent adverse events (AEs) were similar between placebo and AMG 557 arms; most commonly headache and upper respiratory tract infection.
Conclusions: Results from this exploratory placebo-controlled trial in lupus arthritis suggest potential clinical benefit of ICOSL blockade by AMG 557. These data support further clinical trials intervening in this costimulatory pathway in SLE and other autoimmune diseases.
Disclosure of Interest: L. Cheng Shareholder of: Amgen Inc., Employee of: Amgen Inc., Z. Amoura Consultant for: GlaxoSmithKline, AstaZeneca, BristolMyerSquibb, Amgen Inc., B. Cheah Grant/research support from: Merck, F. Hiepe Grant/research support from: Sanofi, Amgen Inc., GlaxoSmithKline, AstaZeneca, Ablynx, Consultant for: Baxalta, AstaZeneca, BristolMyerSquibb, GlaxoSmithKline, Novartix, Miltenyi, Neovacs, Hexal, Neovi, Speakers bureau: Pfizer Inc., Roche, UCB, B. Sullivan Shareholder of: Amgen Inc., Employee of: Amgen Inc., L. Zhou Shareholder of: Amgen Inc., Employee of: Amgen Inc., G. Arnold Shareholder of: Amgen Inc., Employee of: Amgen Inc., W. Tsuji Shareholder of: Amgen Inc., Johnson&Johnson, Consultant for: Celimmune, Seattle Genetics, Resolve