were no unexpected new AEs observed in patients who continued with voclosporin treatment compared to control-treated patients for more than one year.

Table 1. UPCR

	Control (n=100)		Voclosporin (n=116)		Treatment Comparison of Voclosporin to Control	
	n	UPCR (mg/mg)	n	UPCR (mg/mg)	UPCR (mg/mg)	p-value
Pre-treatment baseline, mean	100	3.87	116	3.94	NC	NC
Change from pre-treatment baseline, LS mean						
Year 1	100	-2.4	116	-3.0	-0.6	0.0080
Year 2	51	-2.1	73	-3.1	-1.0	0.0004

LS, least squares; NC, not calculated; UPCR, urine protein creatinine ratio.Mixed effects model for repeated measures (MMRM) analysis of LS mean change from pre-treatment baseline for UPCR included terms for baseline covariate, treatment, visit and treatment by visit interaction. Integrated results include data from pre-treatment baseline of AURORA 1, the one-year treatment period in AURORA 1 and up to a one-year treatment period in AURORA 2.

Conclusion: Patients in the voclosporin treatment arm maintained meaningful reductions in proteinuria with no change in mean eGFR at two years of treatment. Additional AURORA 2 efficacy and safety data will be provided at the conclusion of the study.

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POS0682 RETROSPECTIVE ANALYSIS OF PREGNANCY OUTCOMES IN PATIENTS WITH OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (OAPS), NON-CRITERIA OAPS (NC-OAPS) AND ANTIPHOSPHOLIPID CARRIERS

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Background: Antiphospholipid (aPL) antibodies are considered in obstetric morbidity even when Sydney criteria for OAPS are not met. Classification and treatment of NC-OAPS patients and aPL carriers during pregnancy are still debated.
Objectives: To increase knowledge, we evaluated and compared aPL serum profiles, exposure to antithrombotic therapies and pregnancy outcomes in OAPS, NC-OAPS and aPL carrier patients, accessing to our centre.
Methods: A retrospective observational study was conducted on pregnant outpatients from January 2003 to April 2020. According to Sydney revised classification criteria, we considered lupus anticoagulant (LA), IgM and IgG anti-cardiolipin antibodies (aCL), IgM and IgG antibeta2 glycoprotein I antibodies (aβ2-GPI), to stratify aPL risk profiles [Ref]. In each pregnancy, after case stratification into high (≥ 2 aPL or LA serum positivity) versus low (single aPL positivity) risk profile, we evaluated antithrombotic treatment strategy and subsequent pregnancy outcomes as live-births, spontaneous abortions (SA) or foetal losses.
Results: A total of 78 pregnancies were followed: 17 in OAPS, 9 in NC-OAPS and 52 in aPL carrier patients. Rheumatic diseases (RD) coexisted predominately in carriers (73.1%), mainly systemic lupus erythematosus (57.9%). As presented in Table 1, in OAPS and aPL plus RD carrier groups the association of acetyl-salicylic acid (ASA - mean dose 100 mg q.d.) and low-molecular weight heparin (LMWH - mean dose 4000 UI q.d.) showed a better rate of positive outcomes (97.8% of pregnancies) in high aPL risk profile, compared to monotherapy, especially with LA or triple aPL positivity. Conversely, negative outcomes occurred mostly with triple aPL positivity in the first group and double aPL in the second, despite therapy approaches. No significant data were obtained in NC-OAPS group, due to its paucity, though adverse outcomes were observed with monotherapy both in high and low risk profiles. Except aPL carriers with RD, in all other low risk subgroups, a prevalence of negative outcomes occurred using ASA alone, without statistical significance (OR 0; p= 0.45). Similarly, considering the whole population, the use of a mono or a combination therapy in high risk subgroups had not a significant correlation with pregnancy outcomes (OR 1.79; 95%CI 0.31-10.15; p= 0.50).
Conclusion: In our study, negative pregnancy outcomes were sporadic, occurring mostly with ≥ 2 aPL positivity. Combination treatment showed better results overall in high aPL risk profile patients, both in OAPS and NC-OAPS or aPL carriers. Though no significant correlation between outcomes and treatments were found, we hinted how aPL-based risk stratification may be useful in adopting personalised therapies to prevent obstetric failures.

REFERENCE:

[1] Miyakis S, et al (2006) International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome. J Thromb Haemost 4:295–306.

Table 1. Population groups, aPL risk profiles, antithrombotic therapies and pregnancy outcomes.

Population group	aPL risk profile	Type/n° of aPL	Therapy (n° of pregnancies)	Pregnancy outcomes
OAPS	**High**	LA	ASA (1)	1 live-birth
			ASA + LMWH (1)	1 live-birth
		2 aPL	ASA + LMWH (3)	3 live-births
		3 aPL	ASA + LMWH (9)	7 live-births
				2 foetal losses
	Low	1 aPL	ASA (2)	1 live-birth
				1 foetal loss
			ASA + LMWH (1)	
				1 live-birth
NC-OAPS	**High**	LA	-	-
		2 aPL	ASA (1)	1 live-birth
			LMWH (1)	*1 SA*
		3 aPL	-	-
	Low	1 aPL	ASA (6)	5 live-births
				1 SA
			ASA + LMWH (1)	
				1 live-birth
aPL carriers without RD	**High**	LA	ASA (1)	1 live-birth
			LMWH (1)	1 live-birth
		2 aPL	ASA (1)	1 live-birth
			LMWH (2)	2 live-births
		3 aPL	ASA (1)	1 live-birth
			ASA + LMWH (3)	3 live-births
	Low	1 aPL	ASA (5)	4 live-births
				1 foetal loss
aPL carriers with RD	**High**	LA	ASA (4)	3 live-birth
				1 foetal loss
			ASA + LMWH (7)	
				6 live-births
				1 SA
		2 aPL	ASA (6)	6 live-births
			ASA + LMWH (4)	2 live-births
				1 SA
				1 foetal loss
		3 aPL	LMWH (2)	2 live-births
			ASA + LMWH (5)	5 live-births
	Low	1 aPL	ASA (8)	8 live-births
			ASA + LMWH (3)	3 live-births

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POS0683 NOVEL STRINGENT OUTCOME MEASURES APPLIED TO THE PHASE 2 AND 3 ANIFROLUMAB TRIALS

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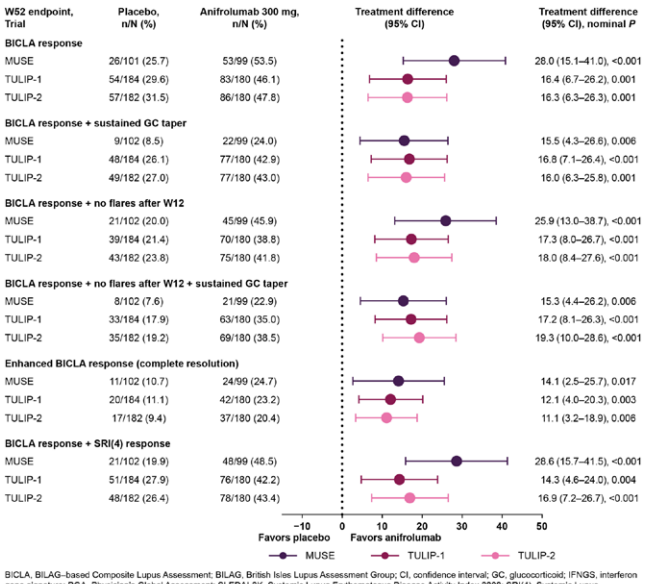
Background: Patients with systemic lupus erythematosus (SLE) who received anifrolumab, a type I interferon receptor antibody, had greater BILAG–based Composite Lupus Assessment (BICLA) response rates vs placebo at Week (W)52 in the phase 2 MUSE[1] and the phase 3 TULIP-1[2] and TULIP-2[3] trials. Patients receiving anifrolumab also had fewer flares, and more patients were able to taper glucocorticoids (GC) vs placebo.[1–3]
Objectives: To evaluate anifrolumab treatment response vs placebo in patients with SLE from MUSE, TULIP-1, and TULIP-2 using more stringent BICLA definitions, as well as a novel endpoint that requires dual BICLA and SLE Responder Index (SRI[4]) responses.
Methods: MUSE (NCT01438489), TULIP-1 (NCT02446912), and TULIP-2 (NCT02446899) were randomized, placebo-controlled, 52-week trials of intravenous anifrolumab (every 4 weeks for 48 weeks) in patients with moderate to severe SLE despite standard therapy.[1–3] Sustained GC taper was defined as taper to ≤7.5 mg/day in patients receiving GC ≥10 mg/day at baseline, or to less than or equal to baseline dose in patients receiving GC <10 mg/day at baseline, achieved by W40 and sustained through W52. Response rates were compared between anifrolumab 300 mg vs placebo groups for patients who **1)** attained a W52 BICLA response with sustained GC taper; **2)** attained a W52 BICLA response and no flares after W12 (flare defined as ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B scores vs the prior visit); **3)** attained a W52 BICLA response with sustained GC taper and no flares after W12; **4)** attained an enhanced BICLA (eBICLA) response at W52 that required complete resolution of all baseline BILAG-2004 activity (all baseline A/B scores to D; no worsening of C or D scores); and **5**) met both BICLA and SRI(4) response criteria.
Results: Evaluated patients received anifrolumab 300 mg (MUSE, n=99; TULIP-1 and TULIP-2, n=180) or placebo (MUSE, n=102; TULIP-1, n=184; TULIP-2, n=182). Response rate differences favoring anifrolumab 300 mg over placebo were observed for all 5 endpoints across MUSE, TULIP-1, and TULIP-2 (Figure 1). A greater proportion of patients had BICLA responses at W52 with sustained GC taper with anifrolumab vs placebo. More patients had BICLA responses at W52 with no flares after W12 with anifrolumab vs placebo. More patients had BICLA responses at W52 with both sustained GC taper and no flares after W12 with anifrolumab vs placebo (treatment difference, 15.3%–19.3%; nominal $P \leq 0.006$). More patients attained eBICLA responses (requiring complete resolution of baseline disease activity) at W52 with anifrolumab vs placebo (treatment difference, 11.1%–14.1%; nominal $P \leq 0.017$). In addition, more patients were dual BICLA and SRI(4) responders at W52 with anifrolumab vs placebo (treatment difference, 14.3%–28.6%; nominal $P \leq 0.004$).
Conclusion: In phase 2 and 3 trials in patients with SLE, anifrolumab treatment was consistently associated with improved disease control vs placebo using stringent endpoint definitions, including BICLA response with sustained GC taper and no flares, an enhanced BICLA response requiring complete resolution of baseline disease activity, and dual BICLA and SRI(4) responses.

Figure. Stringent BICLA response definitions and dual BICLA and SRI(4) response at Week 52 in patients with SLE



BICLA, BILAG–based Composite Lupus Assessment; BILAG, British Isles Lupus Assessment Group; CI, confidence interval; GC, glucocorticoid; IFNGS, interferon gene signature; PGA, Physician's Global Assessment; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SRI(4), Systemic Lupus Erythematosus Responder Index of 4; W, Week.
Rates, differences, 95% CIs, and nominal *P* values were calculated using a stratified Cochran–Mantel–Haenszel approach (stratification factors SLEDAI-2K score at screening, Day 1 GC dose, and IFNGS test status at screening). Response for all endpoints required no trial treatment discontinuation and no use of protocol-restricted medications.
BICLA response, vs baseline: improvement in all BILAG-2004 organ domains (A and B scores to B/C/D and C/D, respectively), no BILAG-2004 domain worsening; no SLEDAI-2K worsening; no PGA worsening (≥0.3 points).
SRI(4) response, vs baseline: reduction ≥4 points in SLEDAI-2K; no new BILAG-2004 organ involvement (≥1 A or ≥2 B items); no PGA worsening (≥0.3 points).

REFERENCES:
[1] Furie R, et al. *Arthritis Rheumatol*. 2017;69:376–86.
[2] Furie RA, et al. *Lancet Rheumatol*. 2019;1:e208–19.
[3] Morand EF, et al. *N Engl J Med*. 2020;382:211–21.

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POS0684 RELATIONSHIP OF ANIFROLUMAB PK WITH EFFICACY AND SAFETY IN PATIENTS WITH SLE

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Background: In patients with systemic lupus erythematosus (SLE), the type I interferon (IFN) receptor inhibitor anifrolumab was well tolerated and was associated with greater percentages of patients with BILAG–based Composite Lupus Assessment (BICLA) responses vs placebo in 2 phase 3 trials: TULIP-1[1] (secondary endpoint) and TULIP-2[2] (primary endpoint).
Objectives: To characterize the relationship of anifrolumab pharmacokinetics (PK) with BICLA response and safety using pooled data from the TULIP trials.
Methods: This analysis included patients with moderate to severe SLE despite standard therapy who had ≥1 dose of investigational product and ≥1 quantifiable PK observation in the randomized, placebo-controlled, 52-week TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) trials of intravenous anifrolumab (every 4 weeks).[1,2] The distributions of average anifrolumab serum concentrations (C_{ave}) during treatment were similar between TULIP-1 and TULIP-2, allowing for data pooling for all analyses. For the exposure–BICLA analysis, the proportions of patients with BICLA responses at Week (W)52 (and corresponding 95% confidence intervals [CIs]) in each quartile/tertile of C_{ave} were compared for anifrolumab 300 mg and placebo groups in all patients, patients who completed treatment, and IFN gene signature (IFNGS) test–high patients who completed treatment, using average marginal effect logistic regression (stratified by SLE Disease Activity Index 2000 total score at screening, IFNGS status at screening, and Day 1 glucocorticoid dosage [mg/day]). The relationships between exposure and key safety events were similarly assessed. Analyses presented focus on the anifrolumab 300 mg dose.
Results: Of the patients in TULIP-1/TULIP-2 who received anifrolumab 300 mg (n=356) or placebo (n=366), 574 completed treatment, of whom 470 were IFNGS test–high at screening. In the exposure–BICLA response analyses, differences favoring anifrolumab 300 mg vs placebo were observed across C_{ave} subgroups among all patients, patients who completed treatment, and IFNGS test–high patients who completed treatment (Table 1). Among IFNGS test–high patients who completed treatment, logistic regression identified C_{ave} as a significant covariate for BICLA response. There was no evidence that the incidence of non-opportunistic serious infections, or increased incidence of herpes zoster (HZ) or infusion-related reactions associated with anifrolumab, were exposure-driven (Figure 1); the incidence of malignancy was low in the anifrolumab 300 mg and placebo groups (<1%), with no evidence that malignancy was exposure-driven through W52.