Obstetrical	Thrombotic	Both
377	320	115
46,3%	39,7 %	14 %

Miscarriages 40%
Fœtal loss 31%
Preeclampsia 12%
IUGR 11%
Multiple type of obstetrical events 10%

The obstetrical manifestations were various as described in figure 2. The number of thrombotic events were 190 arterial and 187 venous. Triple antiphospholipid antibody (tAPL) positivity was found in 20% of patients and lupus anticoagulant (LA) in 22%. No bleeding was registered in 99,6% of cases with treatment by HCQ. HCQ use was associated with favourable outcome in 96% of cases (figure 3).

In multivariate analysis, age more than 65 years was associated with arterial events (odds-ratio 0.13 95%CI 0.03-0.32, p 0.005).

Conclusion: HCQ could be effective in cases of refractory APS but prospective studies are necessary.

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FR10186 HYDROXYCHLOROQUINE ON THE TOP OF STANDARD TREATMENT WITH LOW DOSE ASPIRIN AND LOW MOLECULAR WEIGHT HEPARIN SIGNIFICANTLY REDUCES THE PROBABILITY OF PREGNANCY MORBIDITY IN WOMEN WITH MULTIPLE POSITIVITY FOR ANTI-PHOSPHOLIPID ANTIBODIES

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Background: Hydroxychloroquine is an anti-malarial drug that not only exerts immunomodulatory and anti-thrombotic properties, but also has been shown to reverse several effects mediated by anti-phospholipid antibodies (aPL) in models of obstetric anti-phospholipid syndrome (APS). Not surprisingly, HCQ, whose prescription during gestation is perfectly safe, has been proposed as an additional therapeutic tool in obstetric APS, but evidence of its efficacy is still scant.

Objectives: This study investigates how treatment with HCQ, prescribed in different combinations with low-dose aspirin (LDASA) and low-molecular weight heparin (LMWH), affects the probability of pregnancy morbidity (P_{PM}).

Methods: Data on pregnancies in women with persistent aPL positivity at any titre, with or without autoimmune diseases, were retrospectively collected at a single centre.

A weighted generalized estimated equation (GEE) model was applied to quantify the effect of treatment with HCQ on P_{PM} , allowing to: i) evaluate pregnancy outcomes over time using available longitudinal data; ii) account that pregnancies of the same woman are not independent events; iii) consider that women had a different number of pregnancies; iv) estimate the role of several confounders and predictors.

The model envisaged as dependent variable pregnancy outcome as a binary outcome, defined for each pregnancy as "obstetric complication yes versus no" (pregnancy loss before 10 weeks, pregnancy loss after 10 weeks, premature birth before 34 weeks, according to updated APS classification criteria).

Results: Three-hundred-eighty-one women were recruited in this study: 155 women with aPL positivity (100 women with positivity for criteria aPL and 55 women with low titer aPL) and 226 women with autoimmune diseases but negative aPL. Data were collected on 847 pregnancies: 458 in women with positive aPL (172 in women with criteria aPL and 286 in women with low titer aPL) and 389 in women with autoimmune disease and negative aPL.

P_{PM} in untreated patients are presented in **Table 1**. **Table 2** reports P_{PM} in women receiving LDASA +/- HCQ, LDASA + LMWH +/- HCQ.

Conclusion: HCQ, when added to LDASA or on the top of standard treatment with LDASA and LMWH, allows to reduce P_{PM} . Most importantly, HCQ plus the combo LMWH + LDASA leads to a significantly

reduction of P_{PM} even in women at highest risk, namely those with multiple criteria aPL positivity.

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Table 1. Probabilities of P_{PM} in untreated women with or without aPL.

	P_{PM}
aPL negative	38% (29-48)
Low titer single aPL positivity	62% (52-71)
Low titer double aPL positivity	83% (75-89)
Criteria single aPL positivity	80% (71-87)
Criteria multiple aPL positivity	89% (81-94)

Data are expressed as P_{PM} (95% confidence interval).

Table 2. Probabilities of P_{PM} in treated women with aPL.

	LDASA	LDASA + HCQ	LDASA + LMWH	LDASA + LMWH + HCQ
Low titer single aPL positivity	31% (23-41)	21% (14-30)	15% (9-23)	10% (6-17)
Low titer double aPL positivity	57% (47-66)	44% (35-54)	34% (26-44)	24% (17-33)
Criteria single aPL positivity	52% (42-62)	40% (31-50)	30% (22-40)	21% (14-30)
Criteria multiple aPL positivity	69% (59-77)	57% (47-66)	47% (38-57)	35% (26-45)

Data are expressed as P_{PM} (95% confidence interval).

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PRELIMINARY EXPLORATION OF NEW METHODS TREAT TO PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: REGULATING TH17/TREG CELL BALANCE BY RAPAMYCIN AND ALL-TRANS RETINOIC ACID

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Background: Helper T cells 17 (Th17) and regulatory T cells (Treg) are two important immunoregulatory cells that act in opposite directions¹. Previous study² has shown that Th17/Treg cell balance is one of the important pathogenesis of systemic lupus erythematosus (SLE). Further researches³⁻⁵ believed that rapamycin (RAPA) alone or in combination with all-trans retinoic acid (ATRA) can regulate Th17/Treg cell balance, and then alleviate the condition of SLE.

Objectives: To investigate effect of the use of RAPA alone or combined ATRA on Th17/Treg cell balance in patients with SLE.

Methods: Seventy patients with SLE (64 females and 6 males, mean age 31.91 ± 10.12 years, mean duration 61.14 ± 53.64 months) in our hospital from March 2016 to June 2018 were enrolled. All of them were in line with the standard of ACR in 1997. The patients were randomly divided into RAPA group (RAPA 0.5 mg/time, twice a week) and RAPA+ATRA group (RAPA and ATRA 10 mg/time, twice a week), 35 cases in each group. All were treated continuously for 24 weeks. The number of Th17

and Treg cells in peripheral blood before treatment and 6, 12, 24 weeks after treatment were measured. The SLEDAI scores and glucocorticoid dosage before and after the treatment were also observed to evaluate the differences of efficacy between the two groups.

Results: At different time in each group, the number of peripheral blood Th17 cells in SLE patients was decreased ($P < 0.05$), the number of Treg cells was increased ($P > 0.05$), the ratio of Th17/Treg cells induced ($P < 0.05$), indicating a restored balance of them. The SLEDAI scores and the dosage of glucocorticoid were decreased significantly ($P < 0.001$). There were no significant differences in the number of Th17 cells, Treg cells, SLEDAI scores and the dosage of glucocorticoid between two groups ($P > 0.05$). Compared with pretreatment, the number of Th17 cells, the ratio of Th17/Treg cells and SLEDAI scores after 24 weeks treatment in SLE patients was decreased in RAPA group ($P < 0.05$). Compared with pretreatment, the SLEDAI scores and the dosage of glucocorticoid after 24 weeks treatment in SLE patients was significantly reduced in RAPA+ATRA group ($P < 0.001$).

Conclusion: Using RAPA or combined with ATRA could improve the condition of SLE patients by regulating Th17/Treg cells balance and reduce glucocorticoid dosage, which provided new directions for the pathogenesis and treatment of SLE.

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(a)

(b)

Figure 1. Changes in the number of Th17 cells (number/ μ l) before and after treatment in the two groups.