



## Arthritis News

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### ORAL CONTRACEPTIVE LINK TO LUPUS FLARE SEVERED

SAN ANTONIO, TEXAS—Oral contraceptive use does not cause disease flare in patients with systemic lupus erythematosus, or lupus, according to research presented this week at the American College of Rheumatology Annual Scientific Meeting in San Antonio, Texas.

Lupus is a chronic disease that causes inflammation of the joints, skin rashes, low blood counts, kidney disease, or inflammation around the heart and lungs. It affects one in every 2,000 people in the U.S., and 90% of those affected are women, many of who are young and in their child-bearing years.

Despite their many potential health benefits—including effective contraception, control of irregular menstrual cycles and osteoporosis prevention—oral contraceptives that contain estrogen are rarely prescribed to lupus patients for fear that estrogen would stimulate the immune system and worsen the disease. To test the hypothesis that oral contraceptives do not increase the risk of severe flares in lupus patients, researchers tracked 183 premenopausal patients, average 30 years of age, from 15 U.S. sites in a randomized double-blind study. Patients were given oral contraceptives (triphasic ethinylestradiol and norethindrone) for twelve 28-day cycles or a placebo. All were evaluated at months one, two, three, six, nine and 12.

Severe flares were rare, occurring in only seven of the 91 subjects using oral contraceptives as compared to seven of the 92 patients on placebo. (Two of the severe flares in the patients in the oral contraceptives group occurred when the patients were not on the medication.) The frequency of mild/moderate flares was also equivalent: 1.41 flares per person in the oral contraceptive group versus 1.40 flares per person in the placebo group. At the end of the 12-month prospective trial, the only one of its kind to date, the combined flare rate for both therapies was the same, supporting the safe use of oral contraceptive in patients with lupus.

“Despite data in mice and anecdotal reports in humans, our study did not find an increase in any type of flare in women with lupus,” said the study’s leaders, Jill P. Buyon, MD, Department of Rheumatology, Hospital for Joint Diseases of New York University School of Medicine, New York, NY; and Michelle Petri, MD, MPH, Division of Rheumatology, Department of Medicine, Johns Hopkins University, Baltimore, Maryland. “Because estrogen can increase the risk of blood clots, women with lupus who are at high risk of blood clots because of antiphospholipid antibodies were excluded from this study, and oral contraceptive treatments should not be used in this group of lupus patients.”

The American College of Rheumatology is the professional organization for rheumatologists and health professionals who share a dedication to healing, preventing disability and curing arthritis and related rheumatic and musculoskeletal diseases. For more information on the ACR’s annual meeting, see [www.rheumatology.org/annual](http://www.rheumatology.org/annual).

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*Editor’s Notes: Drs. Buyon and Petri will present this research during a scientific session at the ACR Annual Scientific Meeting from 10:30–10:45 AM CT (11:30–11:45 AM ET) on Monday, October 18, in Ballroom C of the Henry B. González Convention Center. They will be available for media questions during a briefing at 1:30 PM CT (2:30 PM ET) on Monday, October 18, in the on-site Press Conference Room, Room 218.*

## Combined Oral Contraceptives (OC) Are Not Associated with an Increased Rate of Flare in SLE Patients in SELENA

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Despite many potential health benefits, including osteoporosis prevention, oral contraceptives (OC) are rarely prescribed in SLE based on biologic, experimental, epidemiologic and retrospective clinical observations. SELENA (Safety of Estrogen in Lupus Erythematosus-National Assessment) was an equivalence trial to test the hypothesis that OC does not increase the risk of severe flare. Subjects met 1982 ACR criteria for SLE. Patients with a history of thrombosis or moderate/high titer aCL or lupus anticoagulant were excluded. 183 premenopausal patients from 15 US sites (mean age 30 yr) with inactive (76%) or stable/active (24%) disease were randomized double-blind to OC (triphasic 35 µg ethinylestradiol/0.5–1 mg norethindrone) for twelve 28-day OC cycles (N = 91), or to placebo (N = 92). All patients were evaluated at months 1, 2, 3, 6, 9 and 12. 37% were Caucasian, 34% African American, 16% Hispanic and 13% Asian.

The primary endpoint, severe flare (defined by SELENA-SLEDAI), was rare, occurring in 7 of 91 (7.7%) OC subjects vs 7 of 92 (7.6%) for placebo. The 12-month severe flare rate was 0.084 for OC and 0.087 for placebo (log-rank P = 0.90), or a difference in severe flare rates of -0.0025 (95% CI: -0.088, 0.083). The data are consistent with an absolute difference in severe flare rates of up to 8.3%, within the parameters of equivalence. Two of the severe flares in the OC arm occurred when patients were not actually taking OC. There was 1 severe renal flare in OC and 4 in placebo. Mild/moderate flares were equivalent: 1.41 vs 1.40 flares/person-year (OC vs placebo), RR = 1.01, P = 0.96. Furthermore, the number of patients experiencing 3 or more mild/moderate flares was equivalent (15% OC vs 16% placebo, P = 0.86). There was no significant difference in the 12-month combined flare rate for OC vs placebo (0.73 vs 0.67, P = 0.42). There was one DVT in the OC arm, one ocular thrombosis and one superficial thrombophlebitis in the placebo arm. One death (placebo) occurred after trial cessation.

OC does not increase the rate of severe or mild/moderate flares in SLE. With the exception of women at increased risk for thrombosis, results from the only prospective trial to date support the safe use of OC in SLE.

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**Author disclosure legend**—Authors' disclosures of third-party relationships are listed in numeric format according to the following listing:

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