

Hello, my name is Dr Cristina Arriens. I'm a Clinical Associate Member and rheumatologist at the Oklahoma Medical Research Foundation. I am a clinical investigator involved in lupus nephritis and SLE trials, and I will be providing an overview on the poster originally presented at the 2023 LUPUS/KCR meeting entitled:

"Design of 2 phase 3, double-blind, placebo-controlled, global trials of deucravacitinib, an oral, selective, allosteric TYK2 inhibitor in patients with active systemic lupus erythematosus."

The purpose of this video is to aid in the recruitment of the clinical trials being discussed and therefore only focuses on those relevant portions of the poster.

As a background, TYK2, or tyrosine kinase 2, is a nonreceptor tyrosine kinase known to be part of the JAK, or Janus kinase family of proteins.

TYK2 works in pairs or dimers with other JAK proteins to mediate the signal transduction of cytokines important in the pathophysiology of SLE, such as Type I IFN, IL-23, and IL-12.

The POETYK SLE-1 and POETYK SLE-2 are two phase 3, randomized, double-blind, placebo-controlled, global trials in development for the TYK2 inhibitor, deucravacitinib.

The study design for both trials incorporates elements of the previous phase 2 trial, PAISLEY, such as glucocorticoid tapering and a rigorous management structure.

Select inclusion criteria are similar to that of PAISLEY, including:

- Stable background medications
- A SLEDAI-2K score ≥ 6 which must include rash, vasculitis, and/or arthritis
- At least 1 BILAG-2004 Grade A or 2 Grade Bs (one must include the mucocutaneous or musculoskeletal region)
- Seropositivity as measured by ANA $\geq 1:80$ and/or anti-dsDNA and/or anti-Smith

Patients between 18 to 75 years of age with active SLE on background standard-of-care therapy are randomized 1:1 to placebo or deucravacitinib for 52 weeks, with an optional long-term open-label extension of 104 weeks, followed by a safety follow-up period of 4 weeks.

The purpose of these studies is to assess the efficacy, safety, and tolerability of deucravacitinib in patients with active SLE. The safety and efficacy of deucravacitinib for this investigational use has not been established.

The primary endpoint is the proportion of patients who achieve an SRI(4) response at week 52. Additional secondary efficacy and safety endpoints will also be assessed through week 52.

Background therapy is indicated by either 1 antimalarial, 1 immunosuppressant, or both an antimalarial and immunosuppressant.

Patients who are on glucocorticoids at baseline will be instructed to taper to a threshold dose during the double-blind treatment period, unless disease activity is significant.

Randomization in each trial is planned to include 490 patients (245 per double-blind treatment group) in the 29 countries shown here.

This video aims to support recruitment into the POETYK SLE phase 3 trials, which are designed to further evaluate the efficacy and safety of deucravacitinib in patients with active SLE. Accrual into these clinical trials is ongoing.

If you are interested in becoming a study site, please contact Global Trial Manager Carolann Twelves via email at Carolann.twelves@bms.com or visit the links included in the description.

I would like to thank the investigators and patients for making these studies possible.