Methods The IMPACT Study (**IMP**rove **P**regnancy in **A**PS with **C**ertolizumab **T**herapy) is an open label single-stage Phase II trial to evaluate the effect of certolizumab, a TNF-α inhibitor that does not cross the placenta and has been shown to be well tolerated in pregnancy, to reduce the risk of adverse outcomes in this population. Patients with APS and LAC are referred to IMPACT by their physicians, consented and screened remotely by a study investigator, and medication is sent to the patient. They are treated with certolizumab from gestational week 8 through 28. Investigators contact patients every 2 weeks and receive medical reports and research blood samples monthly. The primary outcome is a composite of two APOs associated with poor placentation: fetal death >10 WG or severe preeclampsia/placental insufficiency requiring delivery prior to 34 weeks gestation. The target sample size is 45 evaluable subjects. We hypothesize that the rate of the primary outcome in these pregnancies will be reduced from ~40% based on historical data to 20% with certolizumab.

Results Since May 2017 and despite the COVID-19 pandemic, we have enrolled 41 patients from ten states and 1 Canadian province. Characteristics: 56% previous PE or PI <34 weeks requiring delivery, 83% previous fetal death >10 weeks; 61% thrombosis and/or stroke and 24% SLE in addition to APS. During the trial, no new clinical manifestations of SLE have been observed in participants who did not carry the SLE diagnosis. There were no instances of new anti-DNA antibodies or increases in autoantibody titres in those patients who were anti-DNA antibody positive. ACL or anti-β2GPI antibody titres did not change during the trial. There have been no serious adverse events attributable to the study medication.

Conclusion We are successfully using a "rare disease study" approach to conduct the first trial of a biologic therapy to prevent pregnancy complications in women with APS and LAC. Certolizumab appears to be safe in this small trial. Certolizumab appears to be safe so far in this small trial. IMPACT must be completed before we can draw any conclusions about efficacy, and its results must be confirmed in a future study.

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Lay Summary Pregnancies in patients with antiphospholipid syndrome who have a lupus anticoagulant in their blood have a high likelihood of ending in fetal death or very premature delivery because of poor placental development and preeclampsia. At present, there is no effective treatment for women with these high-risk pregnancies, but our work in an animal model that mimics this human condition shows that blockade of TNF-α, a pivotal mediator of inflammation, prevents adverse outcomes. Our study will determine whether treatment during pregnancy with certolizumab, a TNF-α inhibitor that does not cross the placenta, reduces the rate of poor pregnancy outcomes in women with clinical antiphospholipid syndrome; and, if successful, it will provide a new approach to protecting pregnancies in women with antiphospholipid syndrome and a rationale for trials of TNF-α blockade in women with other conditions, like SLE, who are at risk for preeclampsia or placental insufficiency.

2022 Lupus 21st Century Encore

1202 VOCLOSPORIN FOR LUPUS NEPHRITIS: RESULTS OF THE TWO-YEAR AURORA 2 CONTINUATION STUDY

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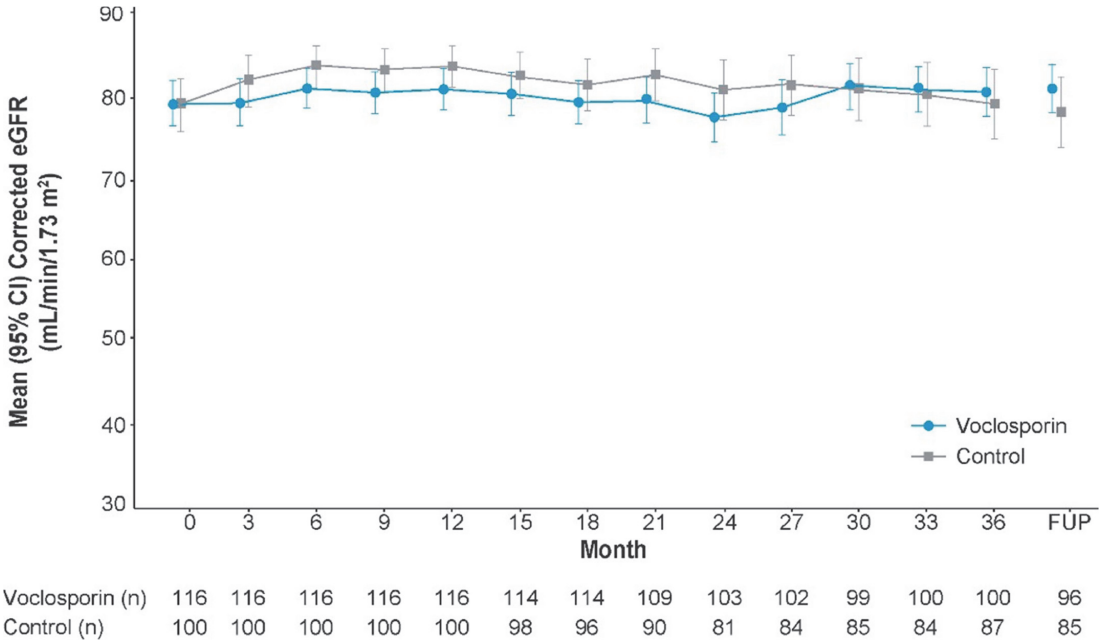
Background Voclosporin (VCS), a novel calcineurin inhibitor, was approved in the US in January 2021 for the treatment of adult patients with active lupus nephritis (LN) in combination with background immunosuppressive therapy. The Phase 3 AURORA 1 study showed that the addition of VCS to mycophenolate mofetil (MMF) and low-dose steroids in patients with LN significantly increased rates of complete renal response at 52 weeks. Here we report the results of the completed continuation study, AURORA 2, which assessed the long-term safety and tolerability of VCS compared to placebo in patients with LN receiving treatment for an additional 24 months following completion of the AURORA 1 study.

Methods Key inclusion criteria for the parent AURORA 1 study included a diagnosis of biopsy-proven active LN (Class III, IV, or V ± III/IV), proteinuria ≥1.5 mg/mg (≥2 mg/mg for Class V) and estimated glomerular filtration rate (eGFR) >45 mL/min/1.73 m^2. Patients who completed AURORA 1 were eligible to enter AURORA 2 to continue on the same blinded therapy as at the end of AURORA 1 (either VCS or placebo twice daily in combination with MMF and low-dose steroids). Safety and tolerability were monitored, and eGFR, serum creatinine (SCr), and urine protein creatinine ratio (UPCR) were also assessed.

Results In total, 116 and 100 patients in the VCS and control arms enrolled in AURORA 2. There were no unexpected safety signals in the VCS arm compared to control, with similar rates of serious adverse events reported in both arms (VCS [18.1%] vs. control [23.0%]; table 1). Eight patients in each arm experienced serious adverse events of infection; serious coronavirus infections were observed in two patients in the voclosporin arm and 5 patients in the control arm. There were 4 and 2 adverse events by preferred term of renal impairment reported in the VCS and control arms, respectively, none of which were considered serious, and no reports of acute kidney injury by preferred term in either arm. There were no deaths in the VCS arm during AURORA 2; four deaths were reported in the control arm (pulmonary embolism [n=1], coronavirus infection [n=3]). Mean eGFR and SCr levels remained stable through the end of AURORA 2. The difference between the VCS and control arms in LS mean change from baseline in eGFR was 2.7 mL/min/1.73 m^2 at 4 weeks following study drug discontinuation (figure 1). The mean reductions in UPCR observed in patients treated with VCS in AURORA 1 were maintained in AURORA 2 with no increase in UPCR noted at the follow-up visit 4 weeks after study drug discontinuation.

Conclusion Voclosporin was well-tolerated over 3 years of treatment with no unexpected safety signals detected. Further,



Abstract 1202 Figure 1 LS Mean eGFR over Time. Analysis of AURORA 2 patients includes data from pre-treatment baseline of AURORA 1, 12 months in AURORA 1 and up to 25 months in AURORA 2 (including 4- week post-treatment visit). Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m2. CI, confidence interval; eGFR, estimated glomerular filtration rate; FUP, follow-up visit (4-week post-treatment visit); LS Mean, least squares mean.

Abstract 1202 Table 1 Overall Summary of Adverse Events

	Control (n=100)	Voclosporin (n=116)
	n (%)	n (%)
Any AE	80 (80.0)	100 (86.2)
Treatment-related AE	21 (21.0)	28 (24.1)
Serious AE	23 (23.0)	21 (18.1)
Serious Treatment-related AE	2 (2.0)	1 (0.9)
AE Leading to Study Drug Discontinuation	17 (17.0)	11 (9.5)
Death*	4 (4.0)	0
Treatment-related Death	0	0

*The four deaths in the control arm were due to pulmonary embolism (n=1) and coronavirus infection (n=3). Includes adverse events starting on or after the first dose of study drug in AURORA 2 up to 30 days after the last dose and all events of death reported during study follow-up. Adverse events were aggregated by System Organ Class and Preferred Term and coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 20.0. AE, adverse event.

eGFR remained stable throughout the study period and the significant and meaningful reductions in proteinuria achieved in AURORA 1 were maintained. These data provide evidence of a long-term treatment benefit of VCS in patients with LN.

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1203 BLOCKADE OF THE MECHANISTIC TARGET OF RAPAMYCIN ELICITS RAPID AND LASTING IMPROVEMENT OF DISEASE ACTIVITY THROUGH RESTRAINING PRO-INFLAMMATORY T CELL LINEAGE SPECIFICATION IN PATIENTS WITH ACTIVE SLE

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Background Systemic lupus erythematosus (SLE) patients exhibit proinflammatory lineage development in the immune system that has been attributed to mechanistic target of rapamycin (mTOR) activation. Moreover, mTOR activation has also been shown in resident cells of tissues affected by end-organ damage. Therefore, safety, tolerance, and efficacy of rapamycin were examined in prospective [1] and retrospective biomarker-driven clinical trials [2,3].

Methods 40 patients having active disease and unresponsive or intolerant to conventional medications were enrolled in a prospective study [1]. Sirolimus was started at 2 mg/day with dosage adjusted to tolerance and 6-15 ng/ml trough levels. Disease activity was evaluated by BILAG, SLEDAI, and prednisone use over 12 months. Blood samples of 56 matched healthy subjects were obtained as controls for