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Humoral Response to COVID Vaccine and Infection is Intact During Sibeprenlimab Treatment of IgAN: Data From the ENVISION Trial

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Objectives : In the ENVISION trial, the APRIL (A Proliferation Inducing Ligand) inhibitor, sibeprenlimab, decreased proteinuria and stabilized eGFR decline in patients with immunoglobulin A nephropathy (IgAN). The substudy reported here evaluated humoral response to SARS-CoV-2 mRNA vaccination and infection.
Methods : Patients enrolled in ENVISION received 12 monthly intravenous infusions of sibeprenlimab or placebo. Recognized COVID infection (AE) and vaccination data were recorded for all patients; for substudy patients, serum SARS-CoV-2 spike and nucleocapsid antibody responses were measured monthly. Response following primary two-dose mRNA COVID vaccination was evaluated. Peak vaccine-induced serum receptor-binding domain (RBD) IgG titers were reported in World Health Organization binding antibody units (BAU)/mL. Retrospective serologic diagnosis of COVID infection required simultaneous elevation of nucleocapsid and spike antibody titers, unexplained by vaccine history.
Results : Among 155 patients who received sibeprenlimab (n=117) or placebo (n=38), 56 (36.1%) had COVID reported as an AE [sibeprenlimab (33.3%), placebo (44.7%)], most of mild severity (Table 1). Two patients (one sibeprenlimab and one placebo recipient) were hospitalized per local protocol, thus considered COVID SAEs. There were no COVID-related deaths, ICU admissions or mechanical ventilation. In the substudy (n=74), symptomatic COVID (reported as an AE) occurred in 47.3% of patients, increasing to 68.9% with addition of retrospective serologic diagnoses. In the substudy cohort, COVID was reported as an AE in 14/15 (93%) of placebo recipients with serologic diagnosis, versus 21/36 (58%) of sibeprenlimab recipients. COVID vaccine seroconversion rates were 100% and peak RBD IgG antibody titers following primary mRNA vaccination exceeded 300 BAU/mL (Fig 1a). Durability of protective RBD IgG titers following vaccination was similar between groups (Fig 1b)
Conclusions : COVID-specific antibody responses to vaccination and infection were preserved in patients with IgAN treated with sibeprenlimab.

Table1. Covid Diagnoses and Severity.jpg

Table 1: COVID Diagnoses and Severity (by AE reporting) and Serologic Diagnosis of COVID Infection

Study Cohort	Sibeprenlimab (2 mg/kg)	Sibeprenlimab (4 mg/kg)	Sibeprenlimab (8 mg/kg)	Sibeprenlimab All patients	Placebo
Entire Study	**n=38**	**n=41**	**n=38**	**n=117**	**n=38**
Any COVID AE, n (%)[a]	11 (28.9)	12 (29.3)	16 (42.1)	39 (33.3)	17 (44.7)
Mild	10 (26.3)	12 (29.3)	13 (34.2)	35 (29.9)	16 (42.1)
Moderate	0	0	3 (7.9)	3 (2.6)	1[d] (2.6)
Severe	1[d] (2.6)	0	0	1 (0.9)	0
Serology Substudy	**n=22**	**n=19**	**n=13**	**n=54**	**n=20**
Any COVID AE, n (%)[a]	8 (36.4)	5 (26.3)	8 (61.5)	21 (38.9)	14 (70.0)
Mild	7 (31.8)	5 (26.3)	7 (53.8)	19 (35.2)	13 (65.0)
Moderate	0	0	1[d] (7.7)	1 (1.9)	1[d] (5.0)
Severe	1[d] (4.5)	0	0	1 (1.9)	0
Asymptomatic, n (%)[b]	6 (27.3)	7 (36.8)	2 (15.4)	15 (27.8)	1 (5.0)
Any COVID diagnosis, n (%)[c]	14 (63.6)	12 (63.2)	10 (76.9)	36 (66.7)	15 (75.0)

[a]Patients with two events were counted only once, with greatest severity recorded.
[b]Retrospective serologic diagnosis, not reported as an AE.
[c]Includes AE and serologic diagnoses (possible for substudy participants only).
[d]Categorized as an SAE.
AE, adverse event; SAE, serious adverse event.

Table1. Covid Diagnoses and Severity.jpg

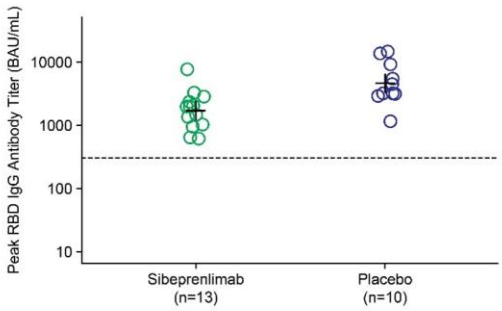

Figure 1a: Peak IgG levels specific to SARS-CoV-2 receptor binding domain of envelope protein (RBD IgG) following primary (two-dose) mRNA vaccination. The geometric mean maximum serum concentration was 1,700 BAU/mL for patients treated with sibeprenlimab (pooled 2, 4, and 8 mg/kg dose levels) versus 4,670 BAU/mL for patients who received placebo (p=0.005). The dashed line indicates 300 BAU/mL, a previously estimated Day-29 post-vaccination RBD BAU/mL level with ~90% vaccine efficacy.[2] Crosses indicate geometric mean. BAU, binding antibody units; IgG, immunoglobulin G; RBD, receptor binding domain.

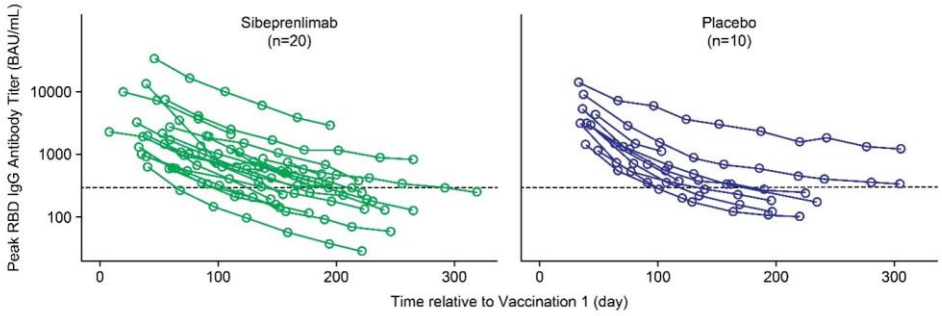

Figure 1b: Decline of RBD IgG antibody titers in sibeprenlimab (pooled 2, 4, and 8 mg/kg dose levels) and placebo recipients following mRNA vaccination (Day 0). Time above the protective threshold titer (300 BAU/mL; dashed line) was consistent between the sibeprenlimab and placebo groups (geometric mean: 192 days, sibeprenlimab; 174 days, placebo). BAU, binding antibody units; IgG, immunoglobulin G; RBD, receptor binding domain.