COVID-19 Prevention With Subcutaneous Administration of the Monoclonal Antibodies Casirivimab and Imdevimab: Subgroup Analysis in Participants with Cardiovascular Disease and Diabetes

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Introduction

- There is an unmet need for treatment options for individuals who are at an increased risk of moderate/severe COVID-19, including those with CVD and/or diabetes.[1]
- The monoclonal antibody combination REGEN-COV™ (casirivimab and imdevimab)[2–4] retains neutralization potency against circulating variants of concern/interest (VOC/VOIs) *in vitro* and *in vivo* and may limit the emergence of treatment resistant variants.[3–6]
- REGEN-COV reduced COVID-19-related hospitalizations or death by approximately 70% (vs placebo) in the Phase 3 portion of a trial in symptomatic outpatients with COVID-19 (COV-2067).[7–8]
- In a Phase 3 prevention trial (COV-2069), REGEN-COV significantly prevented symptomatic SARS-CoV-2 infection vs placebo (81.4% relative risk reduction (RRR); 11/753 (1.5%) vs 59/752 (7.8%), respectively; $P<0.0001$)
  in the primary analysis population (seronegative) and was generally well tolerated.[9]
- Here, we report results of a post-hoc subgroup analysis of patients with CVD (incl. hypertension) and/or diabetes, who are uninfected at baseline and living in the same household as a SARS-CoV-2–infected individual.

Methods

- Uninfected (RT-qPCR-negative) individuals ≥12 years of age were randomized 1:1 to receive a single dose of REGEN-COV 1200 mg SC (600 mg casirivimab and 600 mg imdevimab) or placebo within 96 hours of the index case being diagnosed SARS-CoV-2 positive.
- The trial consisted of a 1-day screening/baseline period, a 28-day EAP (Day 1–29, with dosing on Day 1), and a 7-month follow-up period.
- **Primary endpoint:** The proportion of participants who developed symptomatic infection (COVID-19) during the 28-day EAP among those who were SARS-CoV-2-RT-qPCR-negative and without evidence of immunity (seronegative) at baseline.
- Post-hoc subgroup analyses assessed efficacy in seronegative or sero-overall (regardless of serostatus) participants with CVD and/or diabetes.
- The subgroup analyses were performed using an exact logistic regression model with the fixed categorical effect of treatment group (placebo vs REGEN-COV).
- Data are reported for participants randomized by January 28, 2021, with efficacy assessments excluding participants from an initial administrative assessment. Safety data are reported for participants with CVD and/or diabetes through March 11, 2021.

Results

Study population

- Baseline characteristics of the 366 uninfected (RT-qPCR-negative) and seronegative participants at baseline are presented in **Table 1.**
- Mean age was 55.5 years, 47.8% were male, 83.6% were white, and mean BMI was 31.0 kg/m^2.

Table 1. Baseline characteristics of participants with CVD and/or diabetes (seronegative)

Characteristic	Placebo (n=180)	REGEN-COV 1200 mg SC (n=186)	Total (N=366)
Mean age, years (range)	54.2 (13–92)	56.7 (18–87)	55.5 (13–92)
Male, n (%)	88 (48.9)	87 (46.8)	175 (47.8)
White, n (%)	157 (87.2)	149 (80.1)	306 (83.6)
Black or African American, n (%)	13 (7.2)	20 (10.8)	33 (9.0)
Hispanic or Latino, n (%)	69 (38.3)	60 (32.2)	129 (35.2)
BMI (kg/m^2), mean (SD)	31.2 (6.95)	30.8 (6.17)	31.0 (6.56)

Participants randomized by January 28, 2021.

Efficacy (in those with CVD and/or diabetes)

- In participants with CVD (n=332) or diabetes (n=103), the RRR of developing symptomatic infection (ie, COVID-19; the primary endpoint) with REGEN-COV vs placebo was 54.9% and 69.0%, respectively (**Figure 1**).
- Similar results were observed regardless of whether participants did or did not have CVD and/or diabetes (**Figure 2**).
- Similar results were also observed when the analyses were performed regardless of baseline serology status: 59.6% and 76.3% RRRs for those with CVD and diabetes, respectively.

Figure 1. Cumulative incidence of symptomatic infection by study day in participants with (A) CVD and (B) diabetes (seronegative)

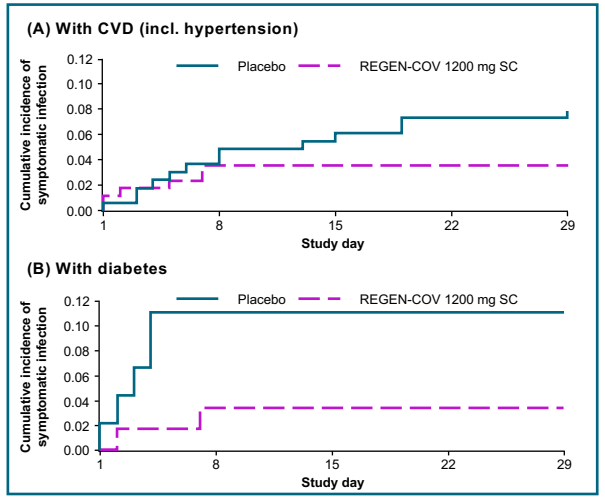
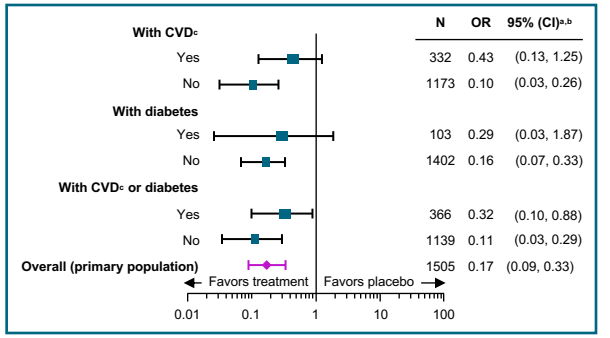


Figure 2. Prevention of symptomatic infection during the 28-day EAP in the primary analysis population (seronegative) and in different subgroups (CVD and/or diabetes; seronegative)



[a]For each subgroup the CI is based on the odds ratio (REGEN-COV group vs placebo group) using an exact logistic regression model with the fixed categorical effect of treatment group. [b]For the overall population, the odds ratio and the CI is based on a logistic regression model adjusted by region (US vs ex-US) and age group (12 to <50 years of age vs ≥50 years of age). [c]Including hypertension.

Safety (in those with CVD and/or diabetes)

- The proportion of participants in the REGEN-COV and placebo groups who experienced ≥1 TEAE was 22.4% vs 32.6% overall, and 17.0% vs 17.7% for non–COVID-19 TEAEs, respectively.
- TEAEs occurring in >2% of REGEN-COV-treated participants with CVD included COVID-19, asymptomatic COVID-19, and injection-site reaction (**Table 2**).
- TEAEs occurring in >2% of REGEN-COV-treated participants with diabetes included injection-site reaction, and COVID-19 (**Table 2**).
- Three participants with CVD and/or diabetes died; a placebo-treated participant on Day 45 (due to cardiac arrest), a REGEN-COV-treated participant on Day 59 (due to congestive heart failure), and a REGEN-COV treated participant on Day 80 (sudden death).

Table 2. TEAEs occurring in >2% of participants[a] in the safety analysis period

Preferred term, n (%)	Placebo	REGEN-COV 1200 mg SC
Participants with CVD	**(n=294)**	**(n=277)**
COVID-19[b]	28 (9.5%)	6 (2.2%)
Asymptomatic COVID-19[b]	26 (8.8%)	16 (5.8%)
Headache	11 (3.7%)	5 (1.8%)
Injection-site reaction	4 (1.4%)	6 (2.2%)
Participants with diabetes	**(n=98)**	**(n=112)**
COVID-19[b]	12 (12.2%)	3 (2.7%)
Asymptomatic COVID-19[b]	8 (8.2%)	2 (1.8%)
Headache	4 (4.1%)	1 (0.9%)
Injection-site reaction	1 (1.0%)	6 (5.4%)

[a]Includes participants who were included in the administrative analyses but excluded from the final efficacy analyses, regardless of SARS-CoV-2 serology status at baseline. [b]The majority of participants who had both asymptomatic infection and COVID-19 had asymptomatic infection first and then subsequently developed COVID-19.

Discussion

- In this trial, which was conducted in the US, Romania, and Moldova, approximately one quarter of participants had CVD and/or diabetes.
- In the setting of this trial — household contacts living with an infected person — we observed a high rate of transmission at a time when the delta VOC was not yet widely circulating: in the placebo arm, 7.8% in the primary analysis population and 9.4% in the CVD and/or diabetes subgroup.
- REGEN-COV treatment prevented symptomatic infection in participants with CVD (55% RRR) and/or diabetes (69% RRR), with effects that were independent of serostatus.
- Despite the increase in vaccination, various groups, including persons with CVD and/or diabetes, are still at risk due to emergence of certain VOCs (eg delta) and the potential for waning of vaccine-induced or natural immunity.
- SC REGEN-COV represents an easy-to-administer option for the prevention of COVID-19 in high-risk persons, as a complement to vaccines.

Summary

- Participants with CVD and/or diabetes are at increased risk of severe COVID-19 disease.[1]
- Treatment with REGEN-COV reduced the risk of developing symptomatic disease, protecting vulnerable groups who have been in contact with an index case.

Conclusions

- Administration of a SC 1200 mg dose of the REGEN-COV antibody combination:
  - Reduced the risk of developing COVID-19 in seronegative participants with CVD and/or diabetes (relative risk reduction range: 55% to 69%), consistent with the overall study results
  - Reduced the risk of developing COVID-19 in participants with CVD and/or diabetes, regardless of serostatus (relative risk reduction range: 60% to 76%)
  - Was generally well tolerated.

Abbreviations: BMI, body mass index; CVD, cardiovascular disease; CI, confidence interval; COVID-19, coronavirus 2019; EAP, efficacy assessment period; OR, odds ratio; RRR, relative risk reduction; RT-qPCR, quantitative reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SC, subcutaneous; SD, standard deviation; TEAE, treatment-emergent adverse event; US, United States; VOC/VOI, variant of concern/interest.

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Additional resources at the Scientific Experience Center