PHASE-2 STUDY OF SAB-185, A POLYCLONAL ANTIBODY TREATMENT FOR COVID-19 IN ACTIV-2/ACTG A5401

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BACKGROUND

High and low doses of SAB-185, a transchromosomic, bovine-derived, fully human polyclonal immunoglobulin product for SARS-CoV-2, were evaluated in an ACTIV-2 sponsored phase 2 randomized placebo controlled trial evaluating the safety and efficacy of investigational agents in non-hospitalized adults with mild-moderate COVID-19. Results of the low dose SAB-185 arm are presented here.

METHODS

Phase 2 comparison of SAB-185 3,840 Units/kg vs placebo (normal saline) administered IV once. Target sample size of 220 (110 active agent, 110 placebo). The comparator group was made up of participants randomized to placebo for SAB-185 3,840 units/kg and participants randomized concurrently to placebo for other agents in the platform trial at the time.

Key inclusion criteria:

- Confirmed SARS-CoV-2 infection in primarily low-risk adults from respiratory sample within 10 days prior to entry.
- ≤ 8 (later' changed to 7) days of symptoms
- Symptoms (not including taste or smell loss) within 24 hours of entry,
- Resting peripheral oxygen saturation ≥92%
- No need for hospitalization per investigator assessment.

Primary outcome measures: 1) SARS-CoV-2 RNA < lower limit of quantification (LLoQ) in nasopharyngeal (NP) swab, 2) time to improvement in targeted symptoms for 2 consecutive days after Day 0, and 3) safety through Day 28.

Secondary outcome measures included: Quantitative NP RNA levels, other symptom-based outcomes, and all-cause hospitalizations and deaths.

Statistical Analysis:

- Modified intent-to-treat population = all participants who initiated an infusion of SAB-185 or placebo.
- Proportion with SARS-CoV-2 RNA <LLOQ was compared between arms using Poisson regression for repeated measures (days 3, 7, and 14), adjusted for day 0 RNA levels.
- Time to first of two consecutive days of symptom improvement was compared using Gehan-Wilcoxon test.
- Proportion with Grade ≥3 adverse events (AEs) was compared using Fisher's exact test.

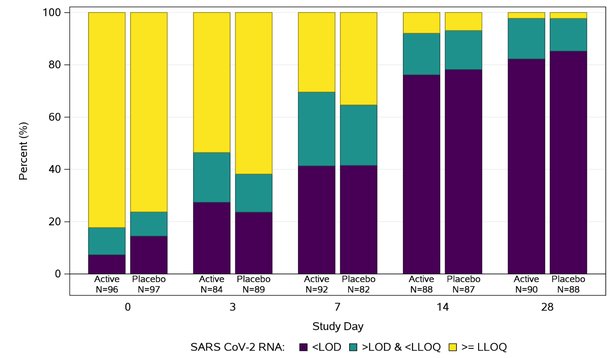
MAIN RESULTS

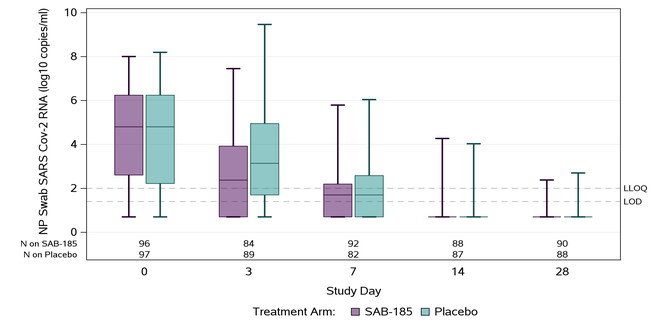
Virology:

At Day 3, median NP RNA levels for SAB-185 and placebo were 2.38 vs 3.14 $\log_{10}$ copies/ml, respectively, (difference in medians = -0.76 $\log_{10}$ copies/ml favoring SAB-185, p=0.10). Based upon this study in primarily low-risk adults, SAB-185 was advanced into a phase 3 clinical trial in non-hospitalized high-risk adults with mild-moderate disease.

No significant differences in the proportion with NP SARS-CoV-2 RNA <LLoQ at Days 3, 7 and 14 (overall p=0.32).

Symptoms: Median (IQR) time to symptom improvement for two consecutive days after Day 0 was 11 (7, 20) days for SAB-185 and 10 (5, 18) days for placebo (p=0.30).





Boxes represent IQR (Q1 to Q3), horizontal line represents median, and bars represent min and max

BASELINE PARTICIPANT CHARACTERISTICS

	SAB-185 (N=107)	Placebo (N=106)	Total (N=213)
Age, years, median (IQR)	38 (31, 49)	39 (29, 48)	38 (30, 48)
Sex, n (%)			
Female	63 (59)	52 (49)	115 (54)
Race, n (%)			
White	90 (85)	94 (89)	184 (86)
Black	9 (8)	6 (6)	15 (7)
Asian	4 (4)	3 (3)	7 (3)
Other[a]	4 (4)	3 (3)	7 (3)
Ethnicity, n (%)			
Hispanic/Latino	45 (42)	61 (58)	106 (50)
Not Hispanic/Latino	62 (58)	45 (42)	107 (50)
Days from symptom onset at study entry, median (IQR)	4 (3, 6)	4 (3, 6)	4 (3, 6)
≤5 days, n (%)	72 (67)	72 (68)	144 (68)
>5 days, n (%)	35 (33)	34 (32)	69 (32)
Risk of COVID-19 progression, n (%)			
Higher risk[b]	14 (13)	9 (8)	23 (11)
Lower risk	93 (87)	97 (92)	190 (89)
History of SARS-CoV-2 Vaccination			
Yes	19 (18)	31 (29)	50 (23)
BMI (kg/m^2), median (IQR)	26.9 (23.3, 30.7)	27.7 (24.6, 31.6)	27.5 (23.6, 31.3)

[a] Other includes Native Hawaiian or Pacific Islander, multiple races, and other
[b] Unvaccinated with age ≥ 60 years and/or presence of high risk condition(s)
IQR = interquartile range; BMI = body mass index

OTHER OUTCOMES

- **No severe infusion reactions, hypersensitivity reactions or drug related serious AEs**
- **Hospitalizations occurred in 2 (2%) SAB-185 and 5 (5%) placebo recipients**
- **No deaths**

CONCLUSIONS

SAB-185 was safe in this phase 2 study of primarily low-risk adults. While no significant differences to placebo were seen in symptom duration and proportion of participants with NP SARS-CoV-2 RNA <LLoQ, quantitative RNA assessments showed a trend towards virologic efficacy at day 3.

ADDITIONAL KEY INFORMATION

Low-dose SAB met pre-specified criteria for evaluation in a phase 3 study, which was subsequently initiated within the ACTIV-2/ACTG A5401 platform trial.

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