POST-ACUTE COVID OUTCOMES: AMUBARVIMAB+ROMLUSEVIMAB VS PLACEBO IN THE ACTIV-2 TRIAL

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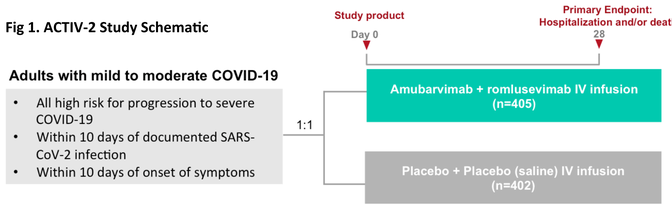
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BACKGROUND

- Whether early antiviral therapy reduces the risk of Long COVID is not known
- The SARS-CoV-2 monoclonal antibodies (mAbs) amubarvimab + romlusevimab (A+R) were highly effective in reducing 28-day all-cause hospitalization/death among high-risk adults with mild-to-moderate COVID-19 in the randomized, placebo-controlled ACTIV-2/A5401 trial (Fig 1)

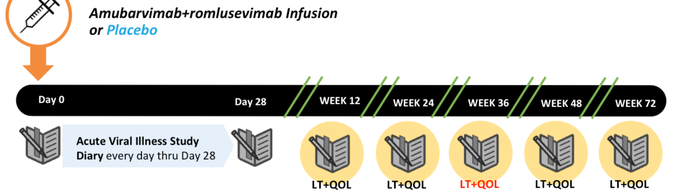
Fig 1. ACTIV-2 Study Schematic



- We assessed the impact of A+R on late outcomes including Long COVID in ACTIV-2

METHODS

- A long-term (LT) symptom diary and 2 health-related quality of life (QOL) questionnaires (EQ-5D-5L and SF-36v2) were completed at week 36 (**Figure 2: Schedule of Events**, below)



- The primary analysis compared the proportion of participants with the composite outcome of self-reported Long COVID (having any COVID-19 symptoms present on a global assessment question in LT diary) at week 36, or hospitalization or death by week 36 between A+R and placebo using modified Poisson regression models with robust variance and inverse probability weighting (IPW) to account for incomplete outcome data
- Supplemental analysis compared the proportion with Long COVID and return to pre-COVID health among those alive, other analyses were restricted to observed data only

Table 1. Baseline Characteristics

	Active (N=405)	Placebo (N=402)	Total (N=807)
Age (years): median (quartiles)	48 (39, 58)	50 (39, 59)	49 (39, 58)
Female sex, n (%)	202 (50%)	207 (51%)	409 (51%)
Cis-gender, n (%)	405 (100%)	400 (100%)	805 (100%)
Race, n (%)			
Black/African American	80 (20%)	61 (15%)	141 (17%)
White	290 (72%)	301 (75%)	591 (73%)
Other	35 (8%)	40 (10%)	75 (10%)
Hispanic/Latino ethnicity, n (%)	203 (50%)	201 (50%)	404 (50%)
BMI (kg/m^2): median (quartiles)	30 (26, 35)	30 (26, 36)	30 (26, 36)
Reporting ≥ 1 high risk co-morbidity, n (%)	379 (94%)	378 (94%)	757 (94%)
Symptom Duration at Study Entry, n (%)			
≤ 5 days	202 (50%)	193 (48%)	395 (49%)
> 5 days	203 (50%)	209 (52%)	412 (51%)
History of SARS-CoV-2 Vaccination, n (%)	30 (7%)	39 (10%)	69 (9%)

Despite being highly effective in preventing all-cause hospitalizations and deaths, ***there was no meaningful effect of early SARS-CoV-2 mAb therapy on measures of Long COVID at 36 weeks*** in high-risk outpatients with mild-to-moderate COVID-19

RESULTS

- 807 participants were randomized and received A+R (n=405) or placebo (n=402) from Jan-July 2021 (Fig 1)
- Baseline characteristics are shown (Table 1)
- 70 (17%) on A+R and 93 (23%) on placebo met the primary outcome; 113 (14%) had incomplete data for determining the outcome (Fig 3)
  - Accounting for incomplete data, weighted Risk Ratio [wRR] A+R vs placebo=0.74; 95% CI: 0.56, 0.97; p=0.03*
  - The difference was driven by fewer hospitalizations/deaths in the A+R arm (5%) than placebo arm (13%) (Fig 4)
- **Excluding 12 participants who died by week 36, frequency of Long COVID was 16% for A+R and 14% for placebo (wRR=1.09; 95%CI: 0.75, 1.58; p=0.64**, Fig 3);** 83% of A+R and 78% of placebo reported return to usual pre-COVID health (wRR=0.74; 95%CI: 0.54, 1.02; p=0.07**)
- There were no differences in general physical health status, individual symptoms (Fig 5), number of symptoms reported or distribution of worst symptom severity between arms
- RRs favored the A+R arm on several EQ-5D-5L domains, but none met statistical significance (Table 2)
- No differences were observed on SF-36v2 assessments (Table 3)

Figure 3: Week 36 Long COVID, Hospitalizations, and Death by Amubarvimab+Romlusevimab (Active) vs Placebo Treatment

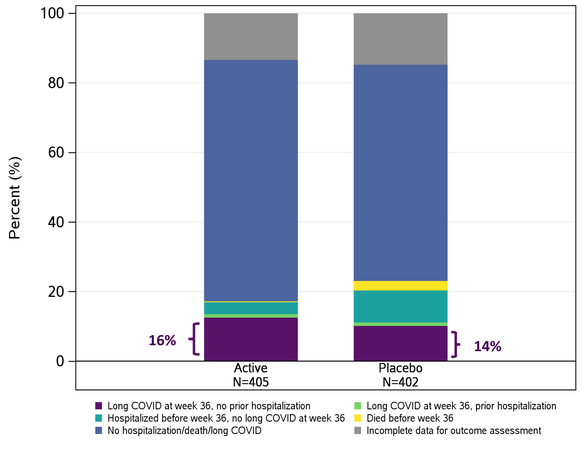
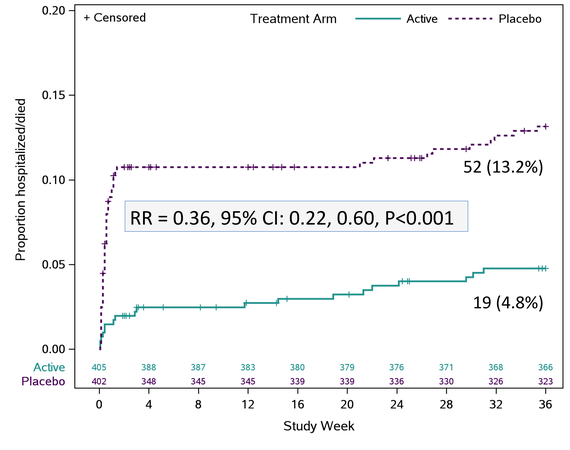


Figure 4. Week 36 Hospitalization and/or Death Cumulative Incidence by Amubarvimab plus Romlusevimab (Active) vs Placebo Treatment



* Weighting model for primary (IPW) analysis of composite endpoint adjusted for time interval, baseline and day 22-28 symptom variable, and interactions with time interval
** Weighting model adjusted for baseline and follow-up variables (including hospitalization status)

Figure 5: Frequency and severity of (a) 13 viral illness Long COVID symptoms and (b) 14 additional Long COVID symptoms reported in participant Long-Term Diary at Week 36 by participants who received Amubarvimab plus Romlusevimab (Active) (n=346) or Placebo (n=321)

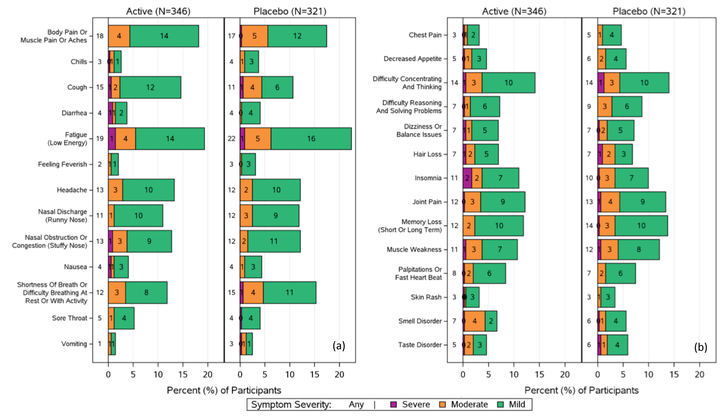


Table 2. EQ-5D-5L Assessments

Assessment, N (%)	Active (N=404)	Placebo (N=391)	Risk Ratio	95% CI	P-value
Self-Care Problems	8 (2%)	15 (5%)	0.52	0.22, 1.20	0.12
Mobility Problems	33 (10%)	43 (14%)	0.74	0.48, 1.14	0.17
Usual Activity Problems	40 (12%)	52 (17%)	0.74	0.51, 1.09	0.13
Pain/Discomfort	83 (26%)	95 (30%)	0.84	0.66, 1.08	0.18
Anxiety/Depression	61 (19%)	54 (17%)	1.09	0.78, 1.52	0.62

Table 3. Medical Outcomes Study-SF-36v2 Assessments

Assessment, Mean (SD)	Active (N=404)	Placebo (N=391)	P-value
Physical Function	88 (21)	88 (22)	0.77
Physical Role	88 (23)	88 (22)	0.82
Bodily Pain	84 (23)	84 (23)	0.74
General Health	79 (20)	80 (19)	0.63
Vitality	71 (22)	73 (22)	0.37
Social Functioning	88 (21)	90 (19)	0.56
Emotional Role	90 (21)	92 (19)	0.25
Mental Health	82 (18)	82 (18)	0.47

CONCLUSIONS

- Prevalence of the primary composite outcome of Long COVID, hospitalization, or death, was lower in the A+R arm vs Placebo, driven largely by early differences in death/hospitalization
- While return to health was reported modestly more commonly in the A+R arm than placebo, no significant differences in rates of Long COVID, symptoms experienced, or quality of life outcomes were observed between arms at 36 weeks after treatment

ADDITIONAL KEY INFORMATION

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More information about ACTIV-2 can be found at www.riseabovecovid.org
Trial Registration: ClinicalTrials.gov Identifier: NCT04518410