A RANDOMIZED CONTROLLED TRIAL OF CAMOSTAT IN OUTPATIENTS WITH COVID-19

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BACKGROUND

- TMPRSS2, a transmembrane protease, is a host factor for cell surface mediated entry of SARS-CoV-2.
- **Camostat**, a protease inhibitor, effectively **inhibits SARS-CoV-1 and SARS-CoV-2 replication *in vitro* by blocking TMPRSS2.**
- **Camostat is an oral, affordable and safe medication**, approved and widely used in Japan and South Korea (for pancreatitis and reflux esophagitis).
- Therefore, we identified camostat as a promising agent for 'repurposing' and for an expedited evaluation in a phase 2 trial of outpatients with COVID-19.

METHODS

- CAMELOT is **a phase 2 randomized, placebo-controlled trial of camostat in adult outpatients with confirmed COVID-19 at risk for severe disease**.
- Participants were **randomized 2:1 to oral camostat (200mg) or matching placebo 4x/day for 14 days**.
- **At least one risk factor for severe COVID-19** was required (age ≥65; hypertension; diabetes mellitus; chronic lung, chronic heart, or chronic liver disease).
- Exclusion criteria were severe liver disease, severe renal impairment, oxygen saturation ≤94% on room air, experimental treatment for COVID-19.
- **Primary efficacy endpoint was hospitalization/death** within 28 days. Secondary efficacy endpoints included positivity for SARS-CoV-2 by PCR on mid-nasal turbinate swabs on days 7 and 15 compared to baseline.

Table 1. Baseline Characteristics of Enrolled Participants (Intent-to-Treat Population)

	Camostat (N=194)	Placebo (N=101)
Female sex	108 (55.7%)	61 (60.4%)
Age, mean years (SD*)	52 (17)	51 (18)
Black or African American	29 (14.9%)	17 (16.8%)
Hispanic or Latino	115 (59.3%)	62 (61.4%)
Risk factor for severe COVID-19		
Hypertension	120 (61.9%)	67 (66.3%)
Chronic lung disease	69 (35.6%)	29 (28.7%)
Diabetes mellitus	48 (24.7%)	27 (26.7%)
≥65 years	44 (22.7%)	22 (21.8%)
Severe obesity	37 (19.1%)	15 (14.9%)
Chronic cardiac disease	25 (12.9%)	9 (8.9%)
≤5 days from symptom onset	149 (76.8%)	76 (75.2%)
Time from positive COVID-19 test, mean h (SD*)	35 (20.7)	32 (21.8)

*SD, standard deviation

Camostat did *not* reduce hospitalizations of outpatients with COVID-19 in the CAMELOT trial. The result was limited by a low overall event rate. There was a modest trend towards faster viral clearance in the camostat group.

RESULTS

- From 11/2020 to 3/2021, 295 participants were randomized (194 to camostat, 101 to placebo; **Table 1**), 76% were ≤5 days from symptom onset, 57% female, 15.6% Black, 60.0% Hispanic/Latino. Most common risk factor for severe disease was hypertension (63.4%).
- Adverse events occurred in 8.7% (camostat) and 13.1% (placebo), respectively. All serious adverse events were due to COVID-19.
- **Event rate for hospitalization/death** was lower than initially assumed (estimated 15% and 30% for camostat and placebo respectively in the power calculation), with **no significant difference between the camostat** (5.3%) **and placebo group** (6.1%, **Fig. 1**). Additional analyses of 'study completers', 'best/worst case scenarios', 'all missing as failure' yielded similar results.
- Of participants with a positive SARS-CoV-2 PCR test on day 0
  - a higher proportion on camostat than on placebo turned negative on Day 7 (35.3% vs. 23.2%, P=0.077) and on Day 15 (78.2% vs. 65.2%, P=0.049, **Fig. 2**).
  - similarly, individuals on camostat had a higher increase of CT numbers (reflecting a higher decrease of viral load) than on placebo on Day 7 (10.11 vs. 8.06, P=0.118, Fig 3A) and Day 15 (14.94 vs. 13.97, P=0.380, Fig. 3B).

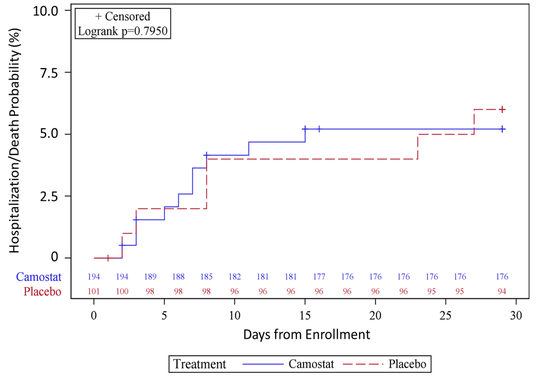


Figure 1. Probability for Hospitalization/Death Over Time (Intent-to-Treat Population)

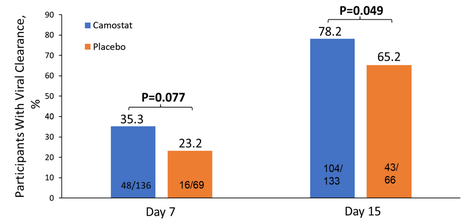


Figure 2. Viral Clearance. Shown are the proportions of participants (As treated population) in the camostat and placebo group on day 7 and day 15 who have cleared viral loads on those days compared to day 0.

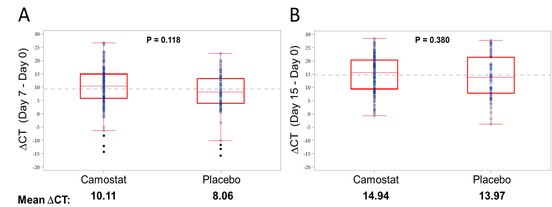


Figure 3. Change in CT Values. (A) Change from Day 0 to Day 7, (B) change from Day 0 to Day 15. Shown is the difference between the CT numbers for SARS-CoV-2 RNA from mid-turbinate nasal swabs for follow-up and baseline for individual participants, e.g., for (A), $y=CT_{d7}-CT_{d0}$. CT, cycle threshold. The assay limit of detection for the Abbott M2000 SARS-CoV-2 qRT PCR was set to 31.5 cycles. P values obtained by Wilcoxon rank-sum test.

CONCLUSIONS

- Camostat is safe in outpatients with COVID-19.
- With a lower than anticipated event rate, we did not observe that camostat was more effective than placebo in prevention of hospitalizations/deaths in outpatients with COVID-19 at risk for severe disease. This is in line with results on hospitalizations/deaths in non-hospitalized individuals with COVID-19 in ACTIV-2/A5401 (Jilg *et al.* CROI2022, oral abstract LB105) and lack of changes in time to clinical improvement or mortality in hospitalized participants of a Danish study (Gunst *et al.*, Eclinical Medicine 2021).
- There was a modest trend towards faster SARS-CoV-2 clearance on Days 7 and 15 on camostat treatment.

ADDITIONAL KEY INFORMATION

Author Contact Information: Nikolaus Jilg, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, njilg@partners.org; **Funding:** Sagent Pharmaceuticals, Schaumburg, IL. NJ's and PAH's institutions received salary support from Sagent. **Acknowledgements:** we thank the participants who volunteered for the CAMELOT study, all study investigators and study teams. NJ: P30 AI060354, K08AI155173-01A1, **ClinicalTrials.gov:** NCT04583592