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Efficacy of a Polyclonal Ovine Fab (PR020) Against SARS-CoV-2 Infection

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ABSTRACT

Background: Passive immune therapies may be useful in mitigating severe COVID-19. The hamster model has been successfully used to study efficacy of COVID-19 treatments. Our objective with this research is to demonstrate initial efficacy of a new polyclonal ovine Fab raised against the SARS-CoV-2 spike protein (PR020) as a treatment for COVID-19.

Methods: Hamsters were treated with PR020 via intraperitoneal route at a dose of 120 mg/kg or a vehicle control once every 24 hours for 8 days, starting 1 day prior to viral challenge with Victoria/1/2020 SARS-CoV-2. Sampling to detect viral RNA and clinical observations were taken throughout the challenge phase. Necropsy occurred 1 day following the last dose of PR020, and tissues were assessed for histopathology and viral RNA.

Results: Hamsters receiving vehicle alone lost weight more rapidly than the PR020 group ($p<0.05$ Day 4 onward). Clinical illness scores for the PR020 group were lower compared to control animals ($p<0.05$ Day 3 onward). While viral shedding assessed by throat swab did not differ between groups, viral RNA levels in lung tissue were significantly lower in PR020-treated animals ($p<0.05$). PR020-treated animals also showed significantly less pathological changes in the lung compared to controls ($p=0.0022$).

Conclusion: Treatment with PR020 resulted in a positive clinical outcome (e.g., less weight loss and lower clinical signs). While treatment appeared to have little effect in the nasopharynx, there was a positive effect in the lower respiratory tract, with substantially less viral RNA in the lungs of the group given PR020 and a decrease in the lung histopathology, including consolidation.

BACKGROUND

- Passive immunization, which involves the introduction of antigen-specific antibodies to protect and/or treat against infection, is a potential strategy for the treatment of COVID-19.[1–3]
- A Syrian hamster model of COVID-19 has been developed and shown to be suitable for the assessment of interventions designed to prevent COVID-19 infection, transmission and disease.[4]
- PR020 is a polyclonal, ovine-derived Fab fragment raised against the SARS-CoV-2 spike protein. We conducted a study of PR020 in Syrian hamsters to evaluate its potential efficacy as a treatment for COVID-19.

METHODS

Study oversight

- This study was conducted at the UK Health Security Agency, Biological Investigations Group, Salisbury, UK.
- The study was conducted in compliance with the UK Home Office Animals (Scientific Procedures) Act 1986, with licensed individuals performing all practical techniques, and was performed under the authority of a UK Home Office-approved project license.

Study design

- 12 hamsters (golden Syrian; n=6 male; n=6 female) with weights ranging from 105–118 g were allocated to two treatment groups: the Vehicle group (PBS; n=6) and the PR020 group (n=6) (**Table 1**).
- Treatments were administered intraperitoneally on Day -1 and then every 24 hours for a total of 8 days (ie, through to Day 6).
- Viral challenge with Victoria/1/2020 SARS-CoV-2 virus was on Day 0 (ie, the day after the first dose of treatment). The target dose was 5.0×10^4 PFU in 200 µL volume. Virus was back-titrated to confirm the dose administered.

Table 1. Study design

Group	Dose	Route	Dose frequency	Days of dosing (post-infection)
Vehicle (PBS) (n=6)	N/A	Intraperitoneal	Once daily	Days −1 to 6
PR020 (n=6)	120 mg/kg	Intraperitoneal	Once daily	Days −1 to 6

Assessments

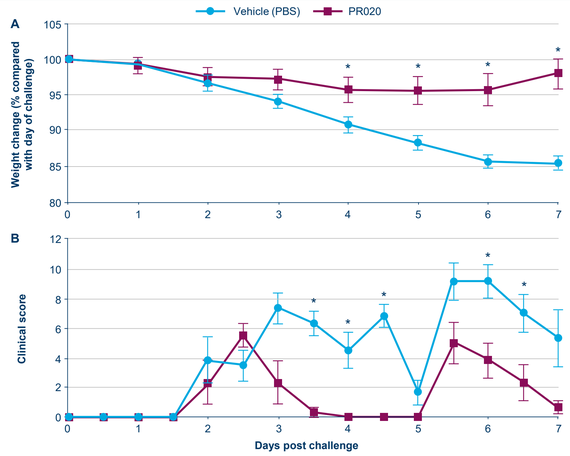
- During the study, body weight and body temperature were measured at least once per day and clinical observations were recorded at least twice per day.
- Clinical scores were assigned a numerical value for analytical purposes:
  - 0: healthy; 2: sunken eyes, ruffled fur; 3: lethargy, wasp-waisted; 5: labored breathing.
- Throat swabs were taken post-challenge on Days 1, 3, 5, and 7, to monitor viral replication in the upper respiratory tract.
- Necropsy was performed on Day 7 and lung and nasal cavity tissues were processed for histopathology. Lung tissue was also processed for quantification of viral load by RT-qPCR of the nucleocapsid gene.

RESULTS

Clinical outcomes

- Post–SARS-CoV-2 challenge, hamsters in the Vehicle group lost weight more rapidly than those in the PR020 group (**Figure 1A**), with the difference reaching statistical significance from Day 4 onwards ($p<0.05$).
- Clinical illness scores of hamsters in the PR020 group were lower than those in the Vehicle group (indicating better health), with statistical significance observed on multiple times from Day 3 post-challenge ($p<0.05$) (**Figure 1B**).

Figure 1. (A) Weight change and (B) clinical scores of hamsters receiving PR020 vs PBS vehicle control

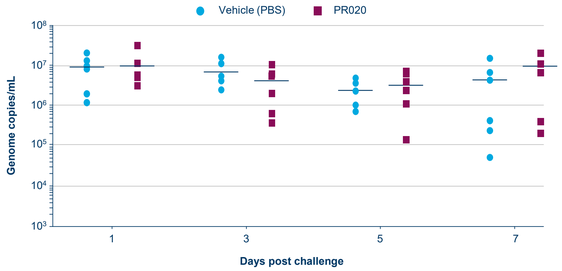


Data are mean (±SE).
*p<0.05 vs PBS vehicle control (Mann–Whitney test).

Viral shedding

- Viral RNA was detected from throat swabs taken on Days 1, 3, 5, and 7 post-challenge, with no statistical difference in viral RNA levels between the PR020 and Vehicle groups (**Figure 2**).

Figure 2. Viral RNA levels in throat swabs of hamsters receiving PR020 vs PBS vehicle control

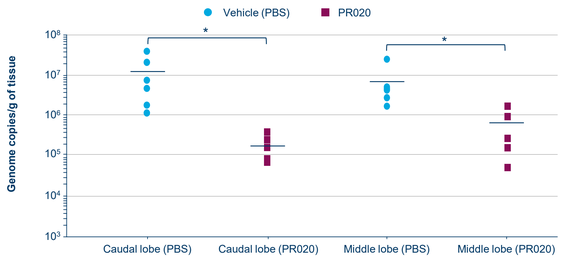


No statistically significant differences were observed between groups (p>0.05 vs PBS vehicle control; Mann–Whitney test).

Viral levels in the lung

- A statistically significant reduction in viral RNA levels in the lungs of hamsters receiving PR020 vs PBS vehicle control was observed on caudal and middle lobe tissue sections (**Figure 3**).

Figure 3. Viral RNA levels in the lungs of hamsters receiving PR020 vs PBS vehicle control

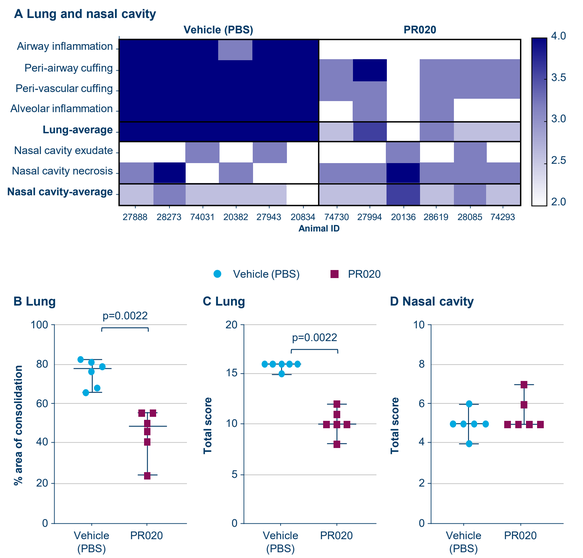


*p<0.05 vs PBS vehicle control (Mann–Whitney test).

Histopathology

- The severity of pathological changes in the lungs was reduced among hamsters receiving PR020 vs those receiving PBS vehicle control (**Figure 4**).
- Pathological changes in the nasal cavity were similar between the PR020 and vehicle control groups.

Figure 4. Histopathology scores: (A) heatmap showing subjective changes in the lung and nasal cavity and average scores for each tissue; (B) lung consolidation scores; and total histopathology scores for (C) the lung and (D) the nasal cavity



Box and whiskers represent median and 95% CI. Significant differences in the total scores between groups (p<0.05) are shown (Mann–Whitney test).

CONCLUSIONS

- **In this animal model study of COVID-19 infection, daily administration of PR020 resulted in a positive clinical outcome, including less weight loss and lower clinical signals.**
- **PR020 appeared to have little effect in the nasopharynx; however, a positive effect of treatment was observed in the lower respiratory tract, with substantially less viral RNA in the lungs of hamsters treated with PR020 vs controls, and a decrease in lung histopathology scores, including consolidation.**
- **Initial findings in this animal model study warrant further investigation of PR020 as a potential treatment for COVID-19 infection.**

Abbreviations

CI, confidence interval; COVID-19, coronavirus disease 2019; PBS, phosphate-buffered saline; PFU, plaque-forming unit; RNA, ribonucleic acid; RT-qPCR, reverse transcription-quantitative polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SE, standard error.

References

1. Cunha LER, et al. iScience 2021;24:103315.
2. Pan X, et al. Antiviral Res 2020;182:104868.
3. Taylor PC, et al. Nat Rev Immunol 2021;21:382–93.
4. Imai M, et al. Proc Natl Acad Sci U S A 2020;117:16587–95.

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Disclosures of interest

ZB, AG, and ED are employees of Protherics UK Ltd. CH and SW are employees of BTG International Inc.

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