Convalescence from prototype SARS-CoV-2 protects Syrian hamsters from disease caused by the Omicron variant

Pre-print:

14th February 2022
Dose-ranging Study initiated Oct 2021

Decreasing doses (PFU) of VIC01 produced a less severe disease in hamsters. Viral shedding from URT (throat swabs) was similar regardless of dose given.

- **% weight change from baseline**
- **Clinical Scores**

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**Viral shedding from URT**

**Clinical Sign** | **Score**
--- | ---
Healthy | 0
Lethargic | 1
Eyes Shut | 1
Behavioural Change | 1
Sunken Eyes | 2
Ruffled | 2
Wasp Waisted | 3
Coughing | 3
Dehydrated | 3
Hunched | 3
Laboured Breathing (1) - occasional catch or skip in breathing rate | 5
Laboured Breathing (2) - abdominal effort with breathing difficulties | 7
Assessment of Humoral Responses

The longitudinal humoral response to VIC01 was high & comparable irrespective of dose

- wt virus (VIC01) neutralisation
- RBD & Spike IgG ELISA
- Spike ADCD

- Omicron emerged ~ 30 DPC
- Opted to re-purpose the study for Omicron re-challenge
Hamster allocation for re-challenge

Re-challenge groups (n=12):

| VIC01 5E+04 | 9328 | M | Victoria |
| VIC01 5E+03 | 23369 | F |
| VIC01 5E+02 | 26638 | F |
| VIC01 1E+02 | 7121 | M | Victoria |
| VIC01 1E+02 | 33027 | M |
| VIC01 1E+02 | 20956 | F |
| VIC01 1E+02 | 3271 | F |
| VIC01 1E+02 | 12056 | F |
| VIC01 1E+02 | 8081 | M |
| VIC01 1E+02 | 4456 | M | Victoria |
| VIC01 1E+02 | 11947 | M |
| VIC01 1E+02 | 14052 | F |
| VIC01 1E+02 | 8694 | M | Omicron |
| VIC01 1E+02 | 16480 | M |
| VIC01 1E+02 | 30243 | F |
| VIC01 1E+02 | 11813 | F | Omicron |
| VIC01 1E+02 | 10913 | M |
| VIC01 1E+02 | 33027 | F |
| VIC01 1E+02 | 4124 | M | Omicron |
| VIC01 1E+02 | 4528 | M |
| VIC01 1E+02 | 10589 | F |
| VIC01 1E+02 | 5322 | M |
| VIC01 1E+02 | 13410 | F |
| VIC01 1E+02 | 13657 | F | Omicron |

*day 41 ND$_{50}$ titres, re-challenged at day 50

Single challenge groups (age matched):

| Challenge Virus: |
| VIC01 = 3.10E+03 FFU (target dose 5E+04 PFU) |
| Omicron = 8.18+03 FFU |
Clinical Observations (culls at 7 DPC)

Omicron appeared to produce a milder disease in hamsters and all re-challenged hamsters appeared to be protected.

**VIC01 Omicron**

- Single challenge
- Re-challenge

### Clinical Signs

<table>
<thead>
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Viral Shedding (RT-qPCR)

Re-challenged hamsters experienced rapid clearance of virus from the URT (throat swabs)

single challenge

re-challenge
Viral Load in the Lungs (RT-qPCR)

The viral load in rechallenged hamsters shows protection against both VIC01 and Omicron compared to single challenge hamsters.

CDC N-gene PCR

**Single challenge (7 dpc)**
Significantly ($P \leq 0.0003$) lower viral load in Omicron challenge hamsters compared to VIC01 challenges hamsters

**Rechallenge**
No significant difference between VIC01 and Omicron rechallenge groups
Histopathology - Lung and Nasal Cavity

At day 7, viral load in the lungs of Omicron challenged hamsters was significantly lower. Pathology in the lungs and nasal cavity was found to be milder omicron challenged hamsters.
• Omicron challenge resulted in less severe, but measurable disease

• Convalescence from VIC01 protected against Omicron challenge

• Hamster model has been valuable in COVID-19 vaccine, therapeutic and passive transfer studies.

• Evaluation of countermeasures against Omicron possible
  • Same endpoints; weight change, clinical signs, viral loads, lung/URT pathology
  • Less discriminatory power
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Virus isolation, propagation & characterisation
In vivo team
Sample processing
Molecular virology
Pathology
Immunology

https://epi.tghn.org/covax-overview/enabling-sciences/agility_epi/