PHASE 1 CLINICAL TRIALS OF A Q-GRIFFITHSIN NASAL SPRAY FOR SARS-COV-2 PROPHYLAXIS

554

Henry W Nabeta[1], Maryam Zahin [1], Amanda Lasnik [1], Elizabeth D Cash[1], Xiaoyong Wu[2], Shesh Rai[2], Kathleen Kitterman[1], Lin Wang[3], Sravan Patel[3], Lisa Rohan[3], Sharon Hillier[3], Nobuyuki Matoba[1], Kevin L Potts[1], Gerald Dryden[1], Kenneth E Palmer[1]

[1]University of Louisville, Louisville, KY, USA, [2]University of Cincinnati, Cincinnati, OH, USA, [3]University of Pittsburgh, Pittsburgh, PA, USA

BACKGROUND

- Current vaccines have waning and non- sterilizing immunity against SAR-CoV-2.
- A broad-spectrum topical prophylaxis strategy may protect vulnerable populations in the face of evolving SARS-CoV-2.
- The algal antiviral lectin Griffithsin (GRFT), and an engineered oxidation-resistant variant Q-GRFT bind oligomannose residues in glycoproteins on viral envelopes. They have robust entry inhibitory activity against SARS-CoV variants of concern, in addition to other respiratory viruses with pandemic potential.
- We designed a nasal spray to deliver Q-GRFT to the upper respiratory tract mucosa for on-demand use as a broad-spectrum prophylactic.

METHODS

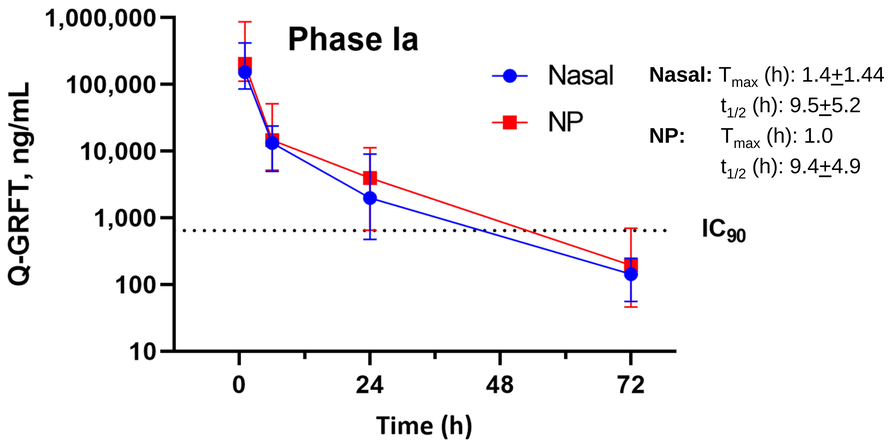
- 18 healthy adult volunteers enrolled in a Phase 1a double blinded, randomized study; Received a single dose of either intranasal Q-GRFT (3.0 mg, 2 sprays per nostril [100 µL/spray]) or placebo at 2:1 ratio.
- Phase 1b study initiated following safety review. 10 volunteers in Group 1 received 3.0 mg once daily, for 7 days; 11 volunteers in Group 2 received 6.0 mg Q-GRFT (3.0 mg twice daily for 7 days).
- Topical Q-GRFT concentrations were measured by ELISA in nasal and nasopharyngeal fluids collected by endoscopy guided swab; plasma drug levels assayed to determine systemic exposure.
- Viral microneutralization cytopathic effect assays performed against SARS-CoV-2 Omicron BA-5 and MERS-CoV.

RESULTS

Table: Demographic characteristics of participants in the study

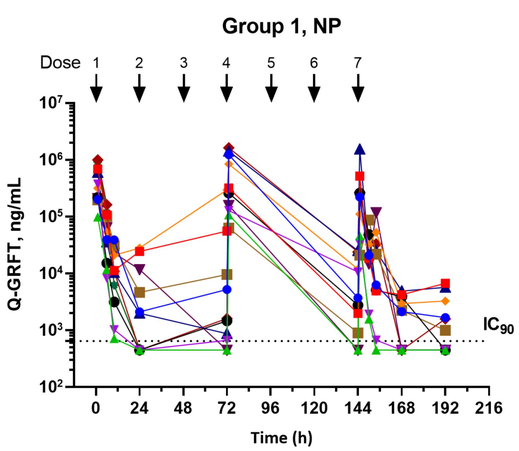
	Age, years, mean (SD)	Gender, n (%)		Race, n (%)	
Phase 1a		Male	Female	White	Non-White
Placebo (N=6)	30.7 (6.65)	3 (50)	3 (50)	2 (33.3)	4 (66.7)
Active (N=12)	33.5 (8.89)	5 (41.7)	7 (58.3)	5 (41.7)	7 (58.33)
Phase 1b					
Group 1	28.5	5 (50.0)	5 (50.0)	4 (40.0)	6 (60.0)
Group2	41.5	6 (54.5)	5 (45.5)	9 (81.8)	2 (18.2)

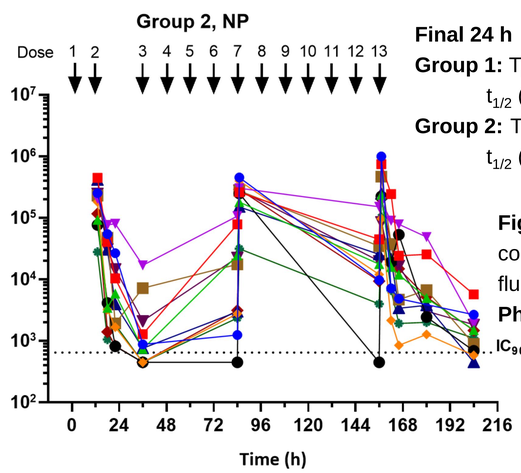
Intranasal Q-GRFT was safe and enhanced mucosal SARS-CoV-2 inhibitory activity in human volunteers.



Nasal: T_{max} (h): 1.4±1.44
$t_{1/2}$ (h): 9.5±5.2
NP: T_{max} (h): 1.0
$t_{1/2}$ (h): 9.4±4.9

Fig. Q-GRFT concentration in nasal and nasopharyngeal fluids collected from participants in Phase 1a study





Final 24 h
Group 1: T_{max} (h): 145.50±1.58
$t_{1/2}$ (h), 3.68±2.11
Group 2: T_{max} (h) 156.9±0.3
$t_{1/2}$ (h): 3.8±3.1

Fig. Q-GRFT concentrations in NP fluids collected in **Phase 1b** study

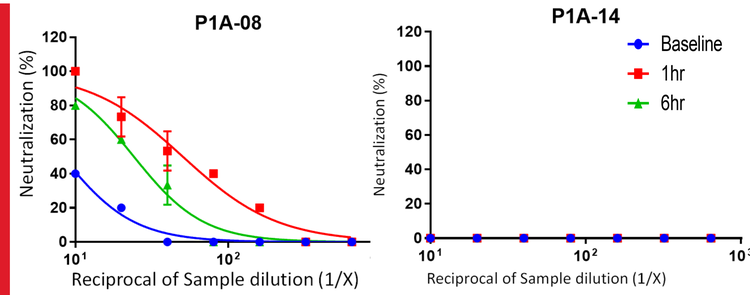


Fig. SARS-CoV-2 Omicron BA-5 neutralization by NP fluids from Q-GRFT treated (L) and placebo (R) participants in **Phase 1a** study.

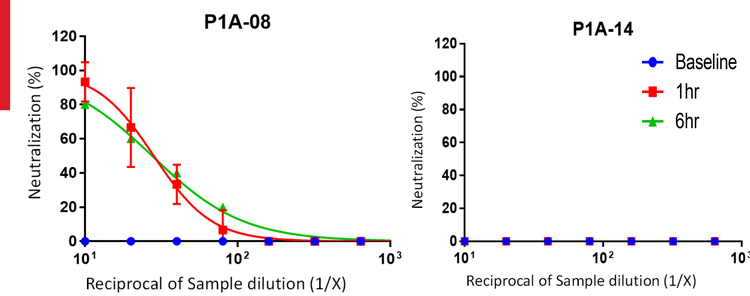


Fig. MERS-CoV neutralization by NP fluids from Q-GRFT treated (L) and placebo (R) participants in **Phase 1a** study.

Safety

- No severe adverse events reported.
- All AEs were mild and related to specimen collection procedures, like eyes tearing and nasal irritation.

CONCLUSIONS

Phase 1a

- Single dose exposure well tolerated
- No product related severe adverse events
- Q-GRFT detected in some subjects up to 24 hours post administration.
- Q-GRFT half life approximately 10 hours
- Intranasal spray enhanced mucosal virus inhibitory activity against SARS-CoV-2 VOC and MERS-CoV

Phase 1b

- Multiple dosing regimen safe and well tolerated
- Robust antiviral activity for at least 6 hours post dosing

ACKNOWLEDGEMENTS

We thank the University of Louisville Clinical Trials Unit for subject recruitment and enrolment.