

Katherine E. Bunge^{1,2}, Lin Wang^{1,2}, Lisa C. Rohan^{1,2}, Sravan Patel,²¹ Leslie Meyn^{1,2}, Ingrid S. Macio², Catherine A Chappell^{1,2}, Amanda B. Lasnik³, Kathleen Kitterman³, Nobuyuki Matoba³, Kenneth Palmer³, and Sharon L. Hillier^{1,2}
¹University of Pittsburgh, Pittsburgh, PA, USA, ²Magee-Womens Research Institute ³University of Louisville, Louisville, KY, USA

BACKGROUND

- The COVID pandemic highlighted the need to develop vaccine alternatives to prevent the spread of SARS-CoV-2, especially in immunosuppressed people.
- Q-GRFT is obtained from a transient expression system in *Nicotiana benthamiana* plants and acts as a broad-spectrum viral entry inhibitor. It binds to oligomannose glycans on viral envelopes and is highly potent, with an IC90 of 645 ng/mL, against the SARS-CoV-2 BA.5 variant.
- A nasal spray formulation was designed to deliver Q-GRFT to the upper respiratory mucosa for topical prophylaxis.
- PREVENT (NCT05180500) was a phase I randomized, double-blind, placebo-controlled study to determine the safety and drug persistence of 14 doses of Q-GRFT intranasal spray (two 100 µL bursts of 7.5 mg/mL Q-GRFT per nostril, 400 µL total).

METHODS

- Healthy, SARS-CoV-2 -vaccinated participants aged 18-55 with normal nasal and pharyngeal exams were randomized 2:1 to either Q-GRFT (n=33) or placebo (n=17).
- Participants initially received one clinician applied metered dose of the study drug and then self administered an additional 13 daily doses after tolerance was established.
- Safety assessments occurred at 1,8,15,21,and 36 days after initial dosing.
- Grade 2 or higher adverse events (AEs) related to study product were compared between groups using Fisher’s exact test.
- Drug persistence was assessed by measuring Q-GRFT concentrations in nasopharyngeal (NP) and nares swabs using ELISA.
- Systemic exposure and immune response were determined by measuring Q-GRFT and antidrug antibody (ADA) concentrations in plasma.
- Acceptability was assessed by questionnaire.

Q-GRFT nasal spray administered for a total of 14 doses was well tolerated and demonstrated persistence up to 24 hours in the upper respiratory mucosa

RESULTS

- Fifty participants (15 male; 35 female) were enrolled from March 22, 2022 to December 31, 2022.
- There was no difference in the proportion of participants with related Grade 2 or higher AEs between groups.(p=0.70) The most frequent AEs were mild nasal irritation and congestion; two participants in the Q-GRFT arm withdrew due to nasal congestion. There were no Grade 3 or higher AEs.
- After adjusting for the dilution factor, Q-GRFT was detected at 50-200X the IC90 in NP and nares swabs at 1 hour and at 1-2X the IC90 at 24 hours after use (Figure); results did not differ by sex.
- ADA was detectable in low levels in plasma in 46% of participants after 14 doses; ADA’s impact on antiviral activity is being assessed.
- No Q-GRFT was detected in plasma samples (lower limit of quantitation: 3 ng/mL).
- Acceptability of the nasal spray (somewhat or highly acceptable) was similar between the two groups (87% Q-GRFT vs. 100% placebo, P= 0.28).

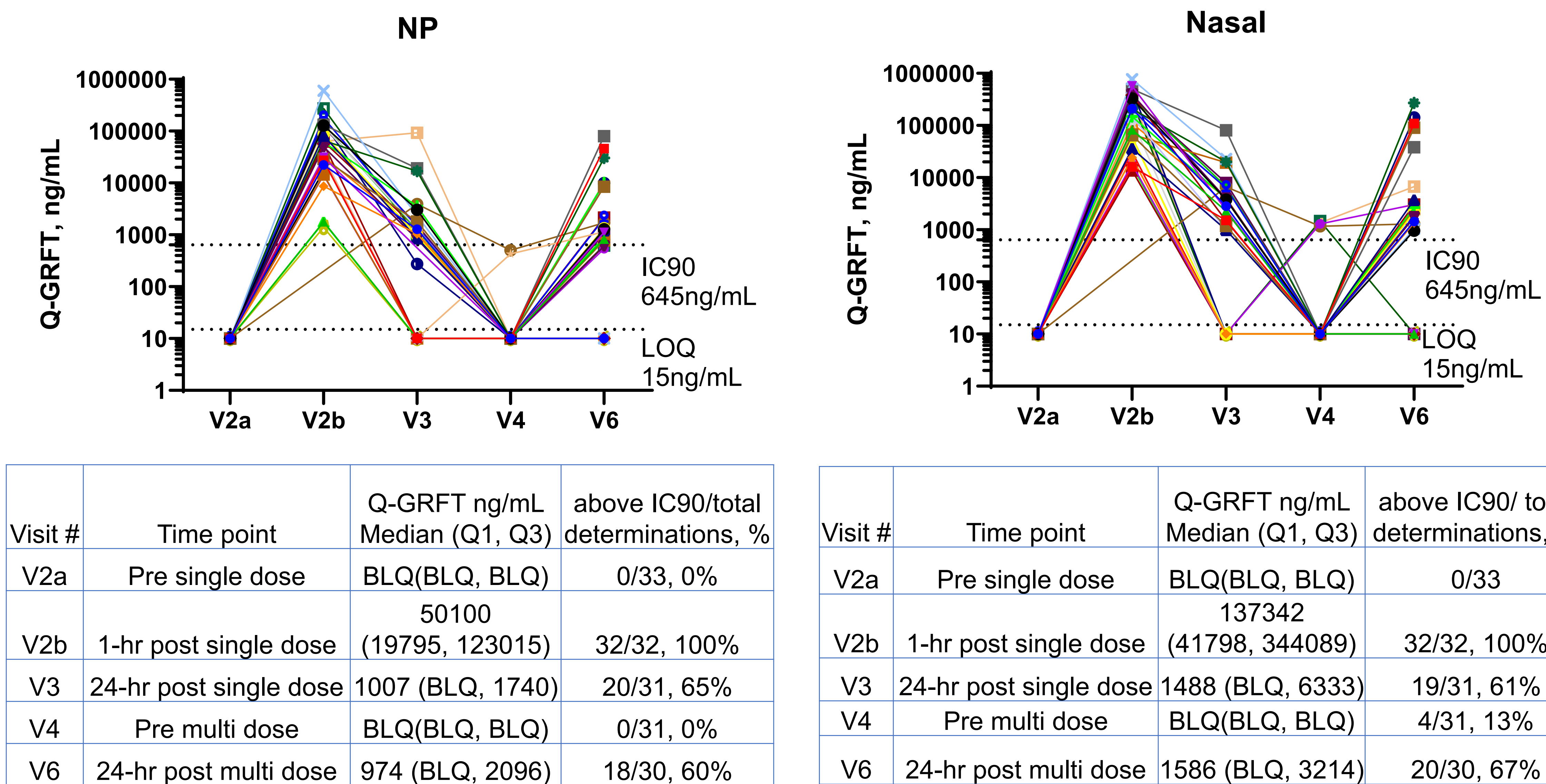


Figure. Q-GRFT Detection in Nasopharyngeal (NP) and Nares Swabs from participants received the active Q-GRFT nasal spray. Data were adjusted by dilution factors reflecting Q-GRFT concentration in collected NP or Nasal fluids. In placebo group, all determinations were below Limit of Quantification (BLQ). Limit of Quantification (LOQ) is 15ng/mL (LOQ)



CONCLUSIONS

- Q-GRFT nasal spray administered for a total of 14 doses was well tolerated and demonstrated persistence up to 24 hours in clinically important anatomic sites without systemic absorption.
- This nasal spray could address the need for an on-demand product for prevention of SARS-CoV-2.
- This product could provide broadly effective antiviral protection in the event of new emergent coronaviruses.
- Q-GRFT inhibits viral entry of all coronaviruses tested, including SARS-CoV, MERS CoV and SARS-CoV-2.
- This product is highly applicable to frontline healthcare workers and at- risk populations, including those that are not responsive to vaccines, such as immunocompromised people.

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