Evaluating Vaxart's oral bivalent GI.1/GII.4 norovirus vaccine in healthy lactating females and their nursing infants: VXA-NVV-108

A phase I, multicenter, randomized, double-blind, placebo-controlled single dose, dose-ranging study to evaluate the safety, tolerability, and immunogenicity of orally administered bivalent GI.1/GII.4 norovirus vaccine in healthy lactating females ≥ 18 years old and their breast-feeding infants

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Conflict of Interest Disclosure

I am a Medical Director employed by Vaxart. As such, I have a financial relationship with the company, which may present a conflict of interest in the context of this presentation.

Norovirus is the leading cause of acute gastroenteritis worldwide

Yearly Global Disease and Economic Burden

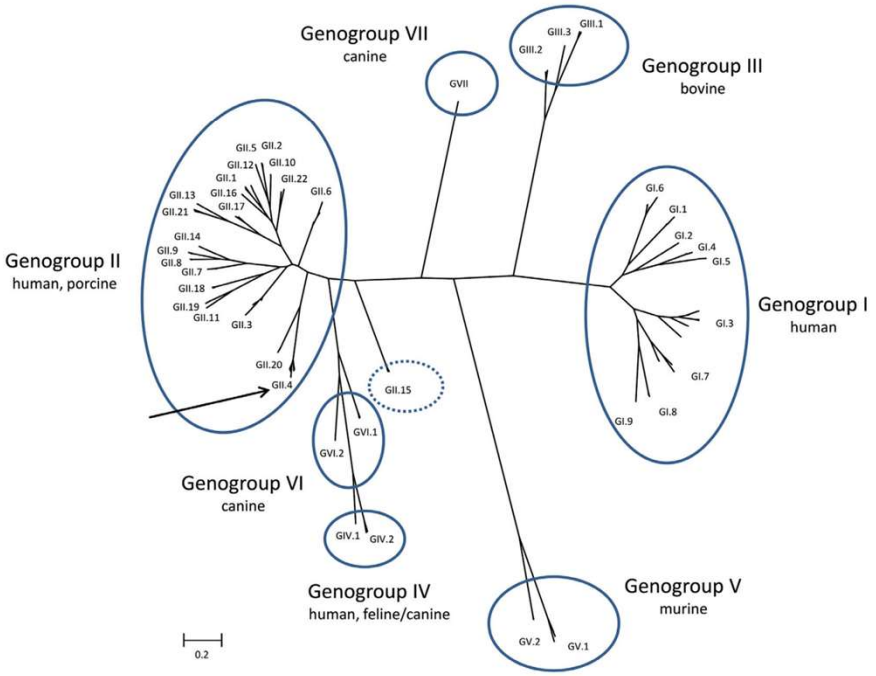
- 699 million norovirus infections
- 219,000 deaths
- $4.2 billon in health system costs
- $60.3 billion in societal costs annually

Risk Groups

- Elderly, young children
- immunocompromised
- Food handlers, travelers and military

Virology

- Several genogroups
  - GI and GII account for the majority of disease in humans
- Virus may be shed for > 4 weeks



Patel MM, Widdowson MA, Glass RI, Akazawa K, Vinjé J, Parashar UD. Systematic literature review of role of noroviruses in sporadic gastroenteritis. Emerg Infect Dis. 2008 Aug;14(8):1224-31. doi: 10.3201/eid1408.071114. PMID: 18680645
Pires SM, Fischer-Walker CL, Lanata CF, et al. Aetiology-Specific Estimates Of The Global And Regional Incidence And Mortality Of Diarrhoeal Diseases Commonly Transmitted Through Food. PLoS One [Internet] 2015 Dec 3;10(12):e0142927
https://www.cdc.gov/norovirus/data-research/index.html
Image from Vinjé J. Advances in laboratory methods for detection and typing of norovirus. J Clin Microbiol. 2015 Feb;53(2):373-81. doi: 10.1128/JCM.01535-14. Epub 2014 Jul 2. PMID: 24989606; PMCID: PMC4298492.

Vaxart Oral Vaccine Solution

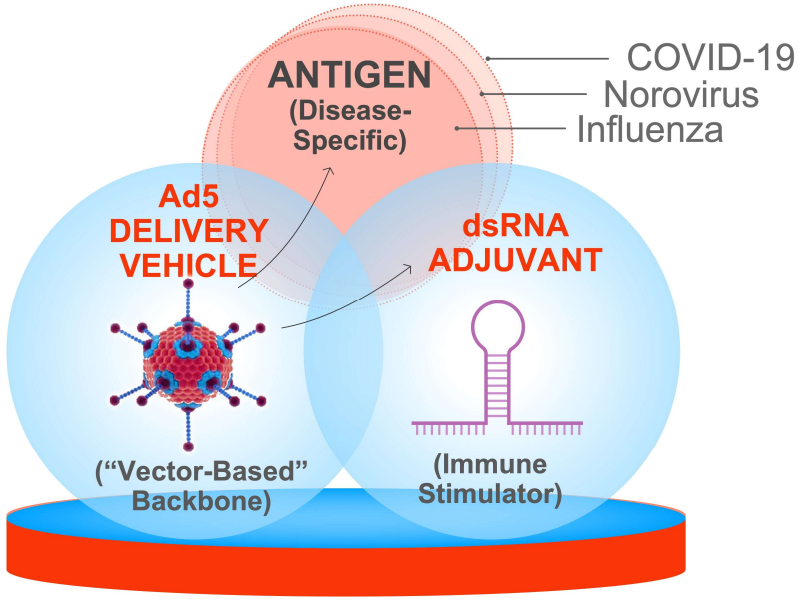
Vector-Adjuvant-Antigen Standardized Technology (VAAST™)

- Modular, Scalable and Standardized Vaccine Creation
- Self Administered Oral Vaccine
- Room temperature stable
- Immunogenic at mucosal surfaces
- Rapidly deployed in a pandemic/outbreak
- Well tolerated and safe
  - 445 subjects exposed to any Vaxart Norovirus vaccine candidate

Vaxart bivalent GI.1/GII.4 norovirus vaccine

- VXA-G1.1-NN: Norovirus GI.1 Norwalk VP1
- VXA-G2.4-NS: Norovirus GII.4 Sydney VP1

Proprietary Oral Vaccine Platform: VAAST™



Background Studies

- Labayo et al.[1] Norovirus-specific immunoglobulin A in breast milk for protection against norovirus-associated diarrhea among infants
  - What is the protective role of NV specific IgA (NV-IgA) in breast milk?
    - Mothers with high positivity rates and titers of NV-IgA in breast milk had NV infected infants with reduced diarrheal symptoms.

- Vaxart, Dr. Stephanie Langel, and Duke University colleagues[2]
  - Oral immunization of lactating ferrets with Vaxart vaccine can provide substantial breast milk antibodies (IgA and IgG) to the vaccine's target disease.

1. Labayo HKM, Pajuelo MJ, Tohma K, Ford-Siltz LA, Gilman RH, Cabrera L, Mayta H, Sanchez GJ, Cornejo AT, Bern C, Dapat C, Nochi T, Parra GI, Oshitani H, Saito M. Norovirus-specific immunoglobulin A in breast milk for protection against norovirus-associated diarrhea among infants. EClinicalMedicine. 2020 Oct 5;27:100561. doi: 10.1016/j.eclinm.2020.100561. PMID: 33043286; PMCID: PMC7536734.
2. Langel, et al, unpublished data

VXA-NVV-108 Study Design: Phase 1 multi-center, double-blind, placebo-controlled single dose, dose ranging study to evaluate the bivalent vaccine safety and immunogenicity

Subjects ≥ 18 y.o. &
Nursing infants >30 days to 11 months of age.

Demographics
- 18-43 yo
- BMI 17.5-54.4 kg/m2
- Race
  - Black/AA (71)
  - Others (5)
    - South African Colored (1)
    - Colored (4)

VXA-G1.1-NN +
VXA-G2.4-NS

High dose
1x10^{11}/strain
30

Medium dose
5x10^{10}/strain
30

Placebo
16

*Image is from South Africa Outline Vectors by Vecteezy
**Image is from Mother Vectors by Vecteezy

Safety Analysis

VAXART

Vaxart's oral bivalent GI.1/GII.4 norovirus vaccine is well tolerated

VXA-NVV-108 Summary of Solicited Adverse Events of Reactogenicity Post-Vaccination (Day 1-Day 8)

	SSx Severity by Treatment Arm						Cumulative SSx by Treatment Arm			All Arms	
	Med Dose N=30		High Dose N=30		Placebo N=16		Med Dose	High Dose	Placebo		
Severity	1	2	1	2	1	2	All (n %)	All (n %)	All (n %)	All	(n %)
Subjects with ≥1 symptom with maximal severity of grades 1-4	15	1	8	5	5	1	16 (53.3%)	13 (43.3%)	6 (37.5%)	35	46.1%
Headache	6	0	4	4	3	1	6 (20.0%)	8 (26.7%)	4 (25.0%)	18	23.7%
Nausea	5	0	5	1	1	0	5 (16.7%)	6 (20.0%)	1 (6.3%)	12	15.8%
Diarrhea	4	0	3	1	1	0	4 (13.3%)	4 (13.3%)	1 (6.3%)	9	11.8%
Malaise/Fatigue	2	0	2	1	2	0	2 (6.7%)	3 (10.0%)	2 (12.5%)	7	9.2%
Abdominal Pain	1	0	1	1	2	0	1 (3.3%)	2 (6.7%)	2 (12.5%)	5	6.6%
Myalgia	2	1	1	1	0	0	3 (10.0%)	2 (6.7%)	0	5	6.6%
Fever	2	0	2	0	0	0	2 (6.7%)	2 (6.7%)	0	4	5.3%
Anorexia	0	0	2	0	1	0	0	2 (6.7%)	1 (6.3%)	3	3.9%
Vomiting	1	0	0	0	0	0	1 (3.3%)	0	0	1	1.3%
Total# of SSx by severity/arm	23	1	20	9	10	1	24	29	11	64	

Severity Grading 1-4: Mild = 1; Moderate = 2; Severe = 3 and Life-Threatening = 4.
There were no solicited symptoms with severity grading of severe or life-threatening.
Percentages were calculated using the number of enrolled subjects in the designated arm as the denominator.
*22/35 subjects reported 1 solicited symptom

Vaxart's oral bivalent GI.1/GII.4 norovirus vaccine is well tolerated

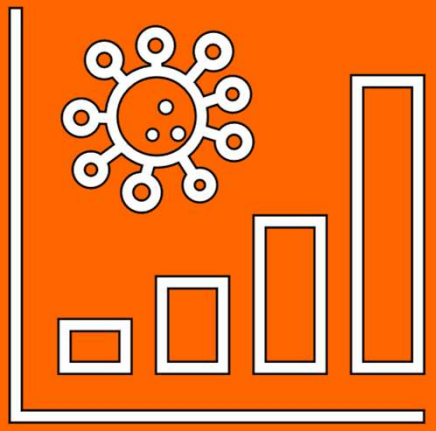
VXA-NVV-108 Summary of Unsolicited Treatment Emergent Adverse Event (Day1-Day 29)

Cohort	Subject	Active Period N=76	Severity	Causality
Medium Dose n=3.3%	1	DIARRHEA	Moderate	Not related
	2	UPPER RESPIRATORY TRACT INFECTION	Mild	Not related
	3	DIARRHEA	Mild	Potential
High Dose n=3.3%	4	BLOODY DISCHARGE FROM RIGHT NIPPLE	Mild	Not related
	5	MYALGIA (LOCALIZED - RIGHT LEG)	Mild	Unlikely
		SORE THROAT	Mild	Unlikely
		DIARRHEA	Mild	Potential
	6	FATIGUE	Mild	Unlikely
Placebo n=12.5%	7	INTERMITTENT HEADACHE	Mild	Potential
	8	HEADACHE	Mild	Potential

The medium dose and high dose arms had 30 subjects each; the placebo arm had 16 subjects. "n" is calculated by the number of subjects in the arm with related AEs divided by the number of subjects enrolled in the designated arm.

- To date, there have been no SAEs, AESIs, NOCIs, TEAEs leading to study discontinuation or withdrawal, severe adverse reactions, or safety signals.

Immunogenicity

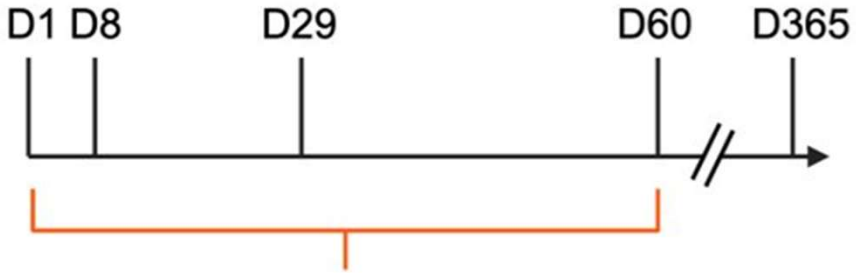


VAXART

Immunogenicity Endpoints: Mucosal and Serum Antibodies

Study Overview:

$5x10^{10}$ IU (medium)
$1x10^{11}$ IU (high)
per strain per dose



Breastmilk
- VP1 specific (GI.1, GII.4) IgA

Serum
- VP1 specific (GI.1, GII.4) IgA, IgG
- Norovirus Blocking Antibody Assay (NBAA)

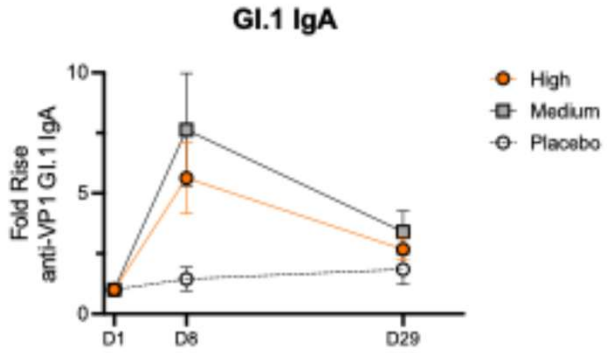
Fecal
- VP1 specific (GI.1, GII.4) IgA

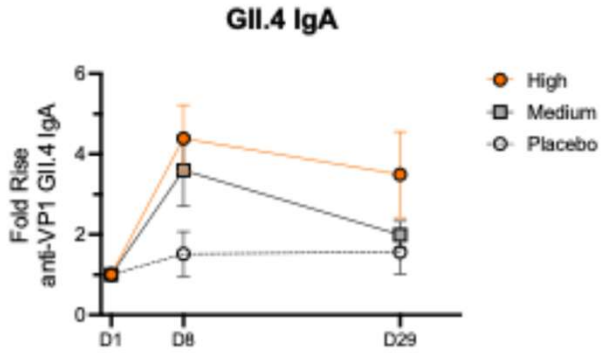
*Image taken from Feeding Vectors by Vecteezy and modified

Serum immune response to oral bivalent GI.1/GII.4 norovirus vaccine

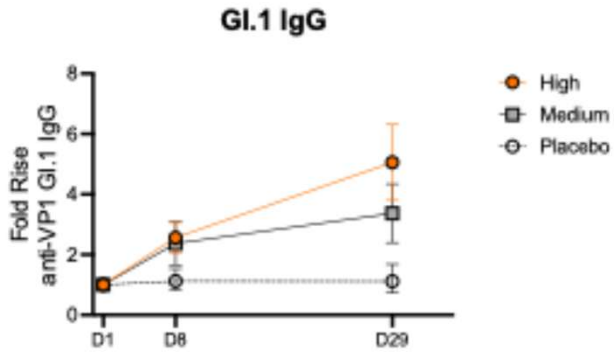
Antibodies in serum remain above baseline through D29

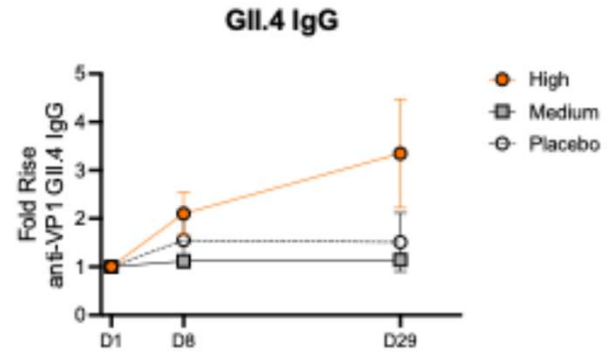
IgA





IgG

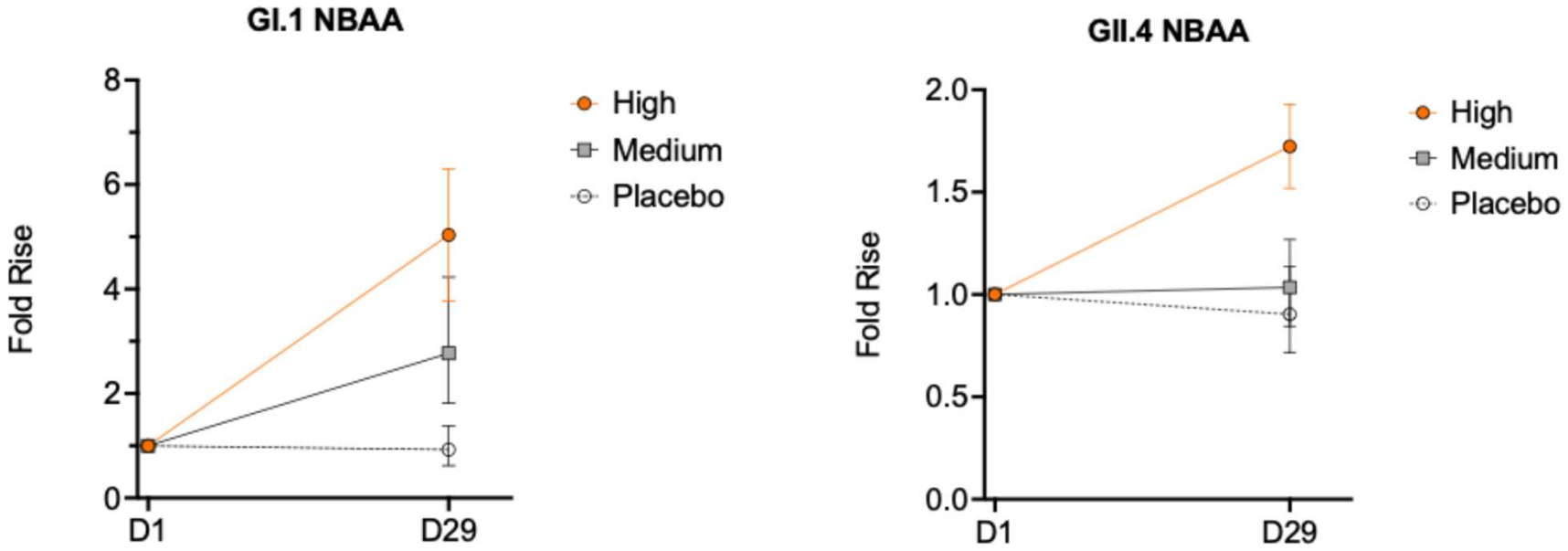




Mean +/- SEM

Serum immune response to oral bivalent GI.1/GII.4 norovirus vaccine

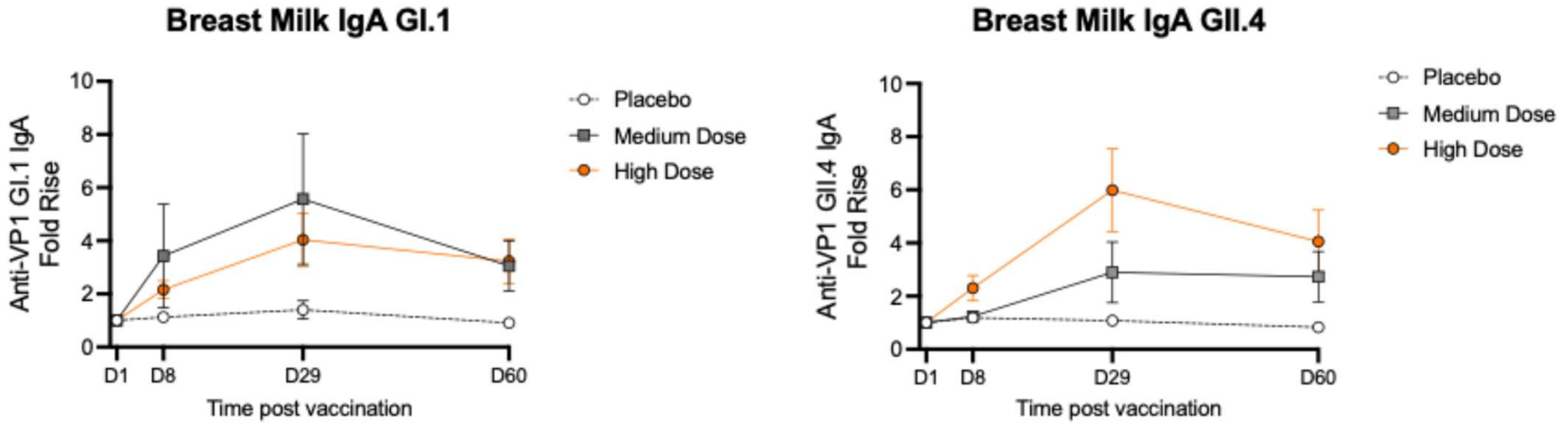
Norovirus Blocking Antibody Assay (NBAA): surrogate assay to measure functionality of serum antibodies



Mean +/- SEM

Breast milk immune response to oral bivalent GI.1/GII.4 norovirus vaccine

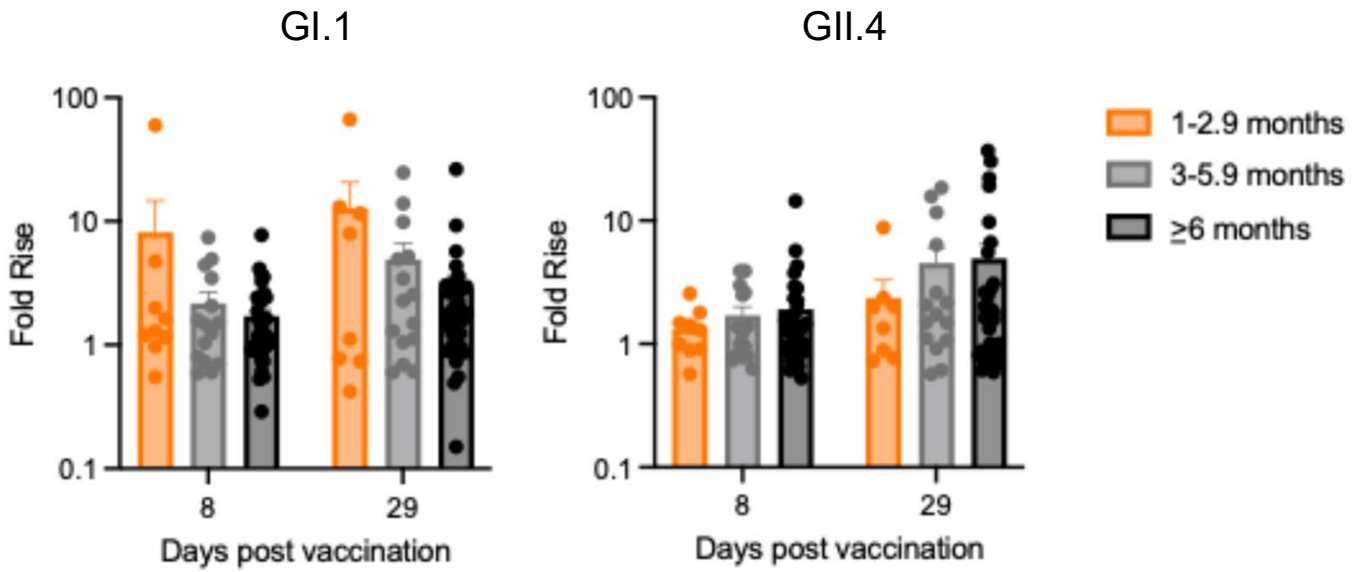
IgA in breast milk increases through D29 post vaccination and remains above baseline through D60



Mean +/- SEM

Breast milk immune response to oral bivalent GI.1/GII.4 norovirus vaccine

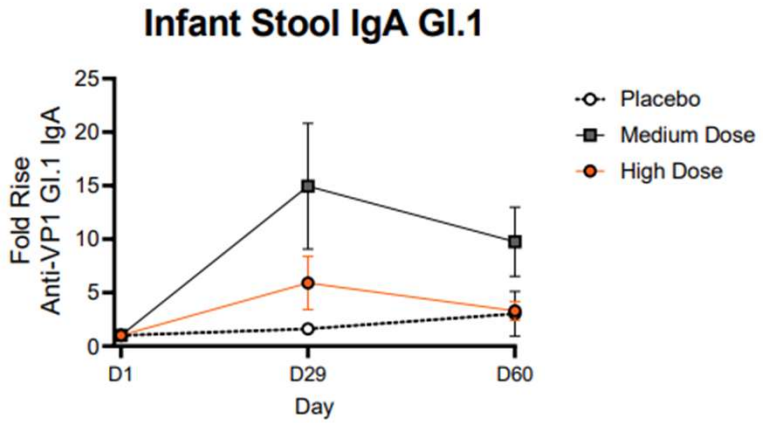
Breast milk IgA induction is not impacted by time of vaccination post birth

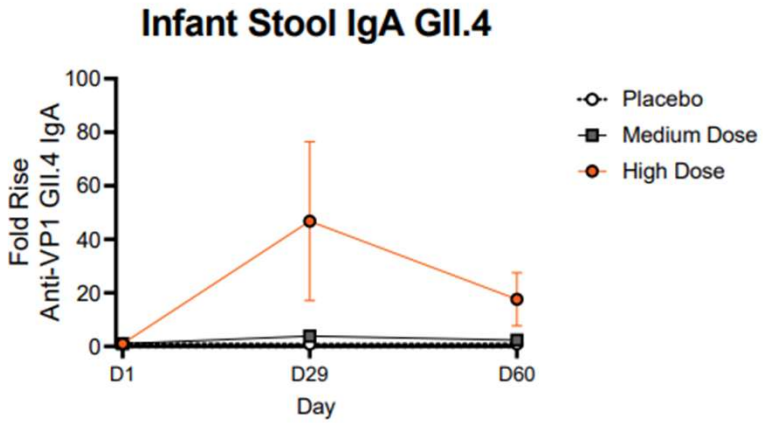


Mean +/- SEM

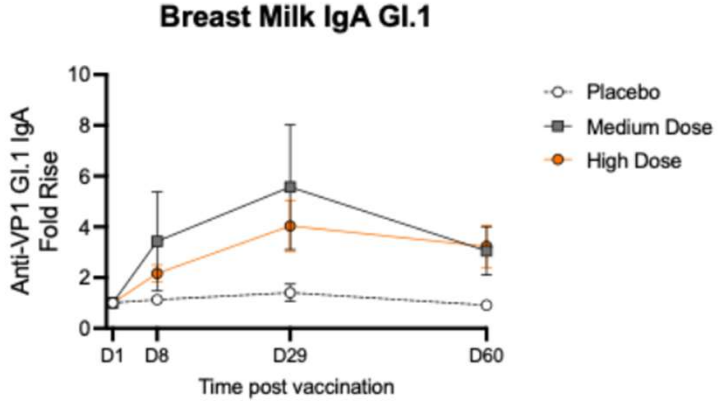
Infant response to breastmilk norovirus antibody

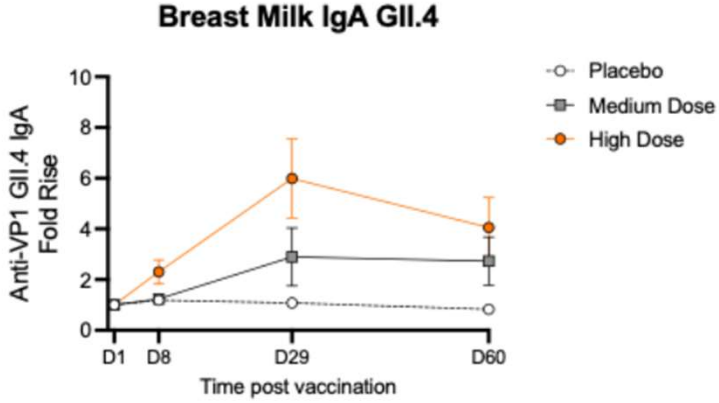
Infant fecal IgA increases through D29 post vaccination and remains above baseline through D60





Infant fecal IgA increase mirrors Breastmilk IgA increase





VXA-NVV-108 Summary

- Safety
  - Vaxart's Bivalent Norovirus GI.1/GII.4 Vaccine side effect profile is similar to placebo and is well tolerated in post-partum, lactating subjects.
    - Solicited and unsolicited AEs are not dose dependent and are similar between active treatment and placebo arms.
    - To date, there have been no SAEs, AESIs, NOCIs, TEAEs leading to study discontinuation, or safety signals.
  - The safety profile aligns with Vaxart's previous clinical trials, which enrolled healthy male and female adult subjects and exposed them to anti-infective candidates built on the VAAST platform.
    - There were no related SAEs, AESIs, NOCIs, TEAEs leading to study discontinuation, or safety signals in all of the completed studies.

VXA-NVV-108 Summary

- Immunogenicity
  - First description of Vaxart's oral tablet vaccine showing immunogenicity in an emerging economy and in breast milk
  - Immunization of lactating women can
    - induce norovirus-specific breast milk IgA
      - Breastmilk IgA remained detectable above baseline through D60
      - Induction of breastmilk IgA responses was not impacted by time post-partum
    - induce norovirus-specific and functional serum antibodies
      - IgA and IgG remained detectable above baseline through D29
      - Induction of functional antibodies was observed to both GI.1 and GII.4
    - induce norovirus-specific fecal IgA in breastfeeding infants
      - Infant fecal IgA remained detectable above baseline through D60
      - The infant fecal IgA trend mirrors the lactating subjects' breastmilk IgA trend

VXA-NVV-108 Summary

- Pending
  - Breast milk and serum immunogenicity through D181 – durability of the immune response
  - Nasal and saliva IgA responses
  - Safety followed through D365

- In conclusion, these results are an important step in the development of a norovirus vaccine that is safe and immunogenic in lactating females with the potential to decrease disease severity in their breastfeeding infants.

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