DMID 21-0012 - Heterologous Platform Boost Study

Mix and Match

Advisory Committee on Immunization Practices
October 21, 2021

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Disclosures:

The speaker receives grant funding from NIAID/IDCRC as co-Chair and site PI for the MixNMatch and as an investigator on the Moderna and Novavax Phase III studies

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Booster Vaccination

	Group	Sample Size	EUA Vaccine	Interval (weeks)	Delayed Booster Vaccination	Strategy Tested
Moderna (100 mcg)	1	50	**Previously dosed Janssen – Ad26.COV2-S**	≥12	Moderna- mRNA-1273	Same Strain Heterologous platform
	2	50	**Previously dosed Moderna – mRNA-1273**	≥12	Moderna- mRNA-1273	Control - Same Strain & platform
	3	50	**Previously dosed Pfizer/BioNTech –BNT162b2**	≥12	Moderna- mRNA-1273	Same Strain Similar platform
Janssen ($5x10^{10}$ vp)	4	50	**Previously dosed Janssen – Ad26.COV2-S**	≥12	Janssen – Ad26.COV2.S	Control - Same Strain & platform
	5	50	**Previously dosed Moderna – mRNA-1273**	≥12	Janssen – Ad26.COV2.S	Same Strain Heterologous platform
	6	50	**Previously dosed Pfizer/BioNTech –BNT162b2**	≥12	Janssen – Ad26.COV2.S	Same Strain Heterologous platform
Pfizer (30 mcg)	7	50	**Previously dosed Janssen – Ad26.COV2-S**	≥12	Pfizer/BioNTech – BNT162b2	Same Strain Heterologous platform
	8	50	**Previously dosed Moderna – mRNA-1273**	≥12	Pfizer/BioNTech- BNT162b2	Same Strain Similar platform
	9	50	**Previously dosed Pfizer/BioNTech –BNT162b2**	≥12	Pfizer/BioNTech – BNT162b2	Control - Same Strain & platform

Study Visits: Days 1, 8 (safety call), 15, 29, Months 3, 6, 12
Blood for immunogenicity studies

Volunteer Characteristics

N = 458

2 Participants
- Group 4 (n = 1)
- Group 6 (n = 1)
- High N protein antibody (D1) suggestive of prior infection

1 Participant
- Group 5 (n = 1)
- Covid-19 Study Day 27

Table 1. Characteristics of the Participants at Enrollment

Group	1	2	3	4	5	6	7	8	9
Primary EUA Immunization Vaccine	Janssen Ad26.COV2-S $5x10^{10}$ vp	Moderna mRNA-1273 100-mcg	Pfizer/BioNTech BNT162b2 30-mcg	Janssen Ad26.COV2-S $5x10^{10}$ vp	Moderna mRNA-1273 100-mcg	Pfizer/BioNTech BNT162b2 30-mcg	Janssen Ad26.COV2-S $5x10^{10}$ vp	Moderna mRNA-1273 100-mcg	Pfizer/BioNTech BNT162b2 30-mcg
Booster	Moderna mRNA-1273 100-mcg			Janssen Ad26.COV2-S $5x10^{10}$ vp			Pfizer/BioNTech BNT162b2 30-mcg		
Total Number	53	51	50	50	49	51	53	51	50
Sex – no. (%)									
Female	26 (49.1)	32 (62.7)	29 (58.0)	27 (46.0)	16 (32.7)	23 (45.1)	29 (54.7)	26 (51.0)	23 (46.0)
Male	27 (50.9)	19 (37.3)	21 (42.0)	23 (54.0)	33 (67.3)	28 (54.9)	24 (45.3)	25 (49.0)	27 (54.0)
Age – years									
Mean (s.d.)	56.8 (14.5)	53.1 (16.2)	54.8 (17.4)	50.1 (13.9)	49.9 (16.8)	50.3 (15.4)	47.7 (14.5)	54.3 (16.8)	50.4 (17.9)
Range	24-81	24-76	22-85	24-77	20-75	20-76	22-74	23-75	19-80
Race – no. (%)									
Asian	4 (7.5)	5 (9.8)	4 (8.0)	3 (6.0)	5 (10.2)	6 (11.8)	1 (1.9)	2 (3.9)	1 (2.0)
Hawaiian or Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)
Black/African American	1 (1.9)	2 (3.9)	3 (6.0)	0 (0.0)	0 (0.0)	2(3.9)	0 (0.0)	2 (3.9)	1 (2.0)
White	46 (86.8)	41 (80.4)	43 (86.0)	44 (88.0)	43 (87.8)	40 (78.4)	50(94.3)	47 (92.2)	43 (86.0)
Multi-racial	1 (1.9)	3 (5.9)	0 (0.0)	3 (6.0)	1 (2.0)	2 (3.9)	1 (1.9)	0 (0.0)	4 (8.0)
Other	1 (1.9%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0%)	0 (0.0)	0 (0.0)	1 (2.0%)
Ethnicity – no (%)									
Non-Hispanic	49 (92.5)	46 (90.2)	47 (94.0)	47 (94.0)	49 (100.0)	48 (94.1)	51 (96.2)	49 (96.1)	45 (90.0)
Hispanic/Latino	4 (7.5)	4 (7.8)	3 (6.0)	2 (4.0)	0 (0.0)	3 (5.9)	2 (3.8)	2 (3.9)	5 (10.0)
Unknown/Not reported	0 (0.0)	1 (2.0)	0 (0.0)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Boost Interval weeks	15.4 wks			18.4 wks			21.5 wks		
Mean (s.d.)	13.7 (1.0)	16.4 (1.9)	16.8 (2.2)	17.7 (2.0)	19.3 (4.2)	20.6 (5.8)	19.9 (2.5)	22.9 (4.6)	24.1 (5.2)
Range	12.0-15.9	12.4-20.0	12.0-20.9	13.9-21.0	12.6-26.0	12.3-41.3	10.9-23.0	12.6-28.7	14.3-31.9

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Immunogenicity

Summary of Available Immunogenicity through D15/D29

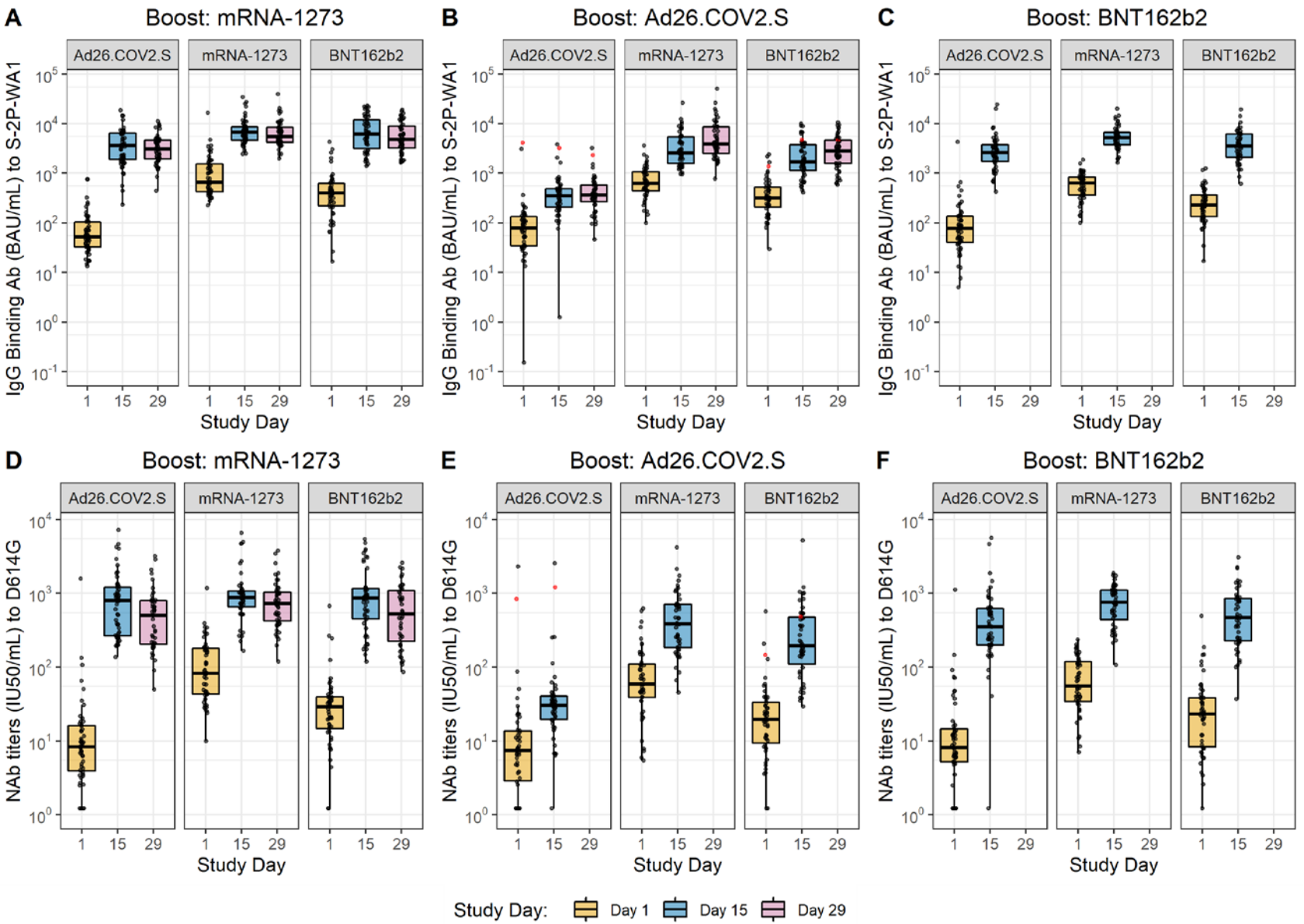
Duke (Montefiori Lab): PsVN (ID50, ID80 and in IU_{50}/mL, IU_{80} /mL)

- D614G N=~450 (50/arm)
- VoCs N=60, 20/arm, 10/age group
  - Beta, Delta - In process

VRC (McDermott Lab): IgG Antibody Binding

- 4-plex (validated) (AU/mL)
  - S-2P (Wa-1 and Beta) N=~450 (~50/arm) (AU/mL)
    - S-2P Wa-1: Binding Antibody Units/mL (BAU/mL) (International Standard)
- 10-plex Fit for Purpose (FFP)
  - S-2P (Alpha, Beta, Gamma, Delta, Wa-1) (AUC/m)

Immunogenicity of all three boosters - IgG binding Antibody (A-C) and Neutralizing Antibody (D-F) Through Days 15/29



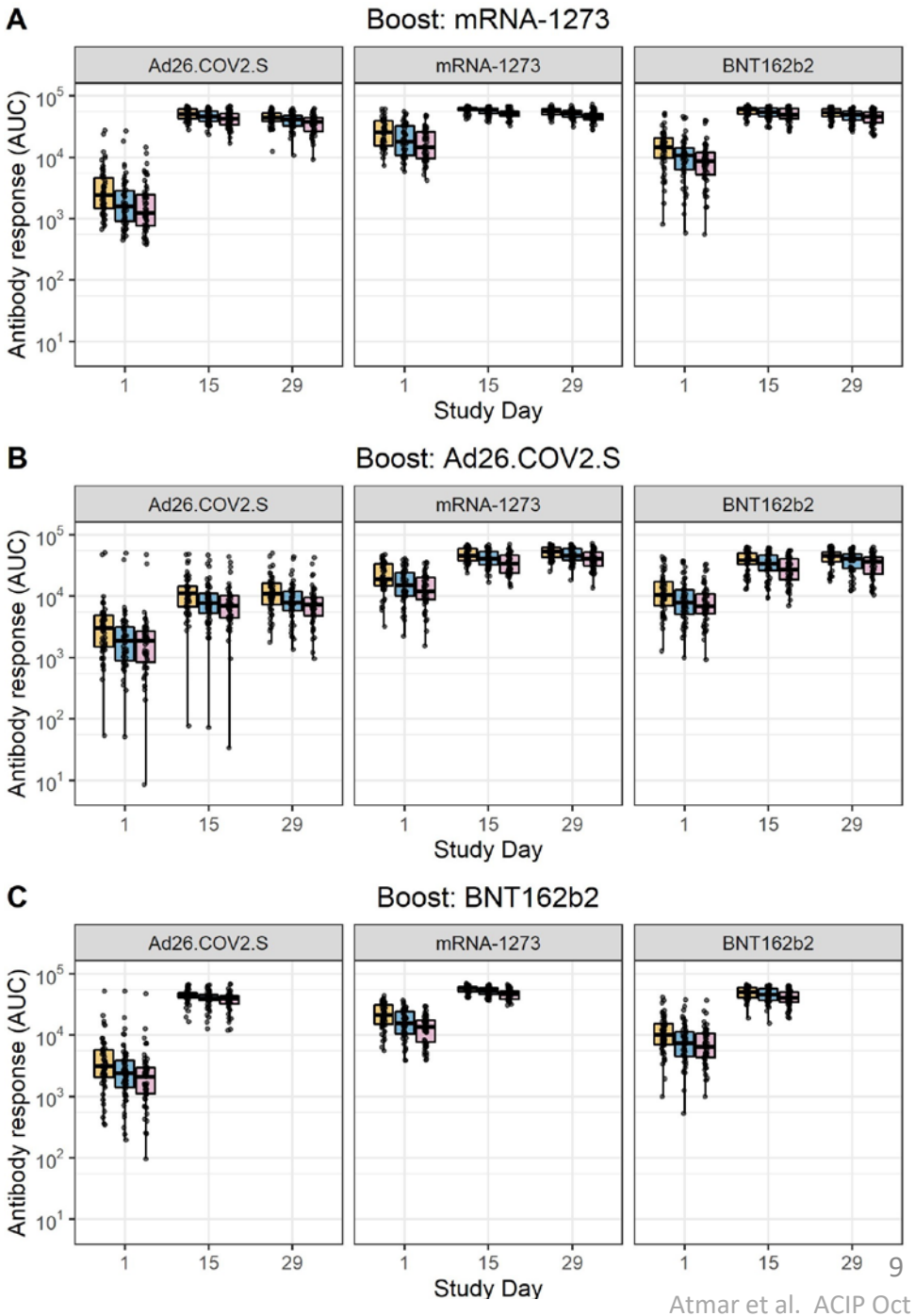
All 3 vaccines

IgG Serum Binding Antibody Response to
S-2P-Wa-1 (control), B.1.1.7 (alpha), and B.1.617.2 (delta)

FFP 10-plex ECLIA, by Group and Timepoint
Results are reported as Area Under Curve (AUC)

Antigen:

- S-2P-WT
- S2-P-B.1.1.7
- S2-P-B.1.617.2



Safety

- Two SAEs
  1. Acute renal failure due to rhabdomyolysis from a fall - Unrelated
     30 days after mRNA-1273 vaccination
  2. Acute cholecystitis - Unrelated
     24 days after Ad26.COV2.S vaccination.

- No pre-specified study-halting rules were met
- No new onset chronic medical conditions occurred (through study D29)
- One related AESI
  - Severe vomiting that led to a medically attended visit the day after vaccination: Ad26.COV2.S boost

Unsolicited AEs (deemed related to boost) of any severity grade

- mRNA-1273: 24/154 (15.6%)
- Ad26.COV2.S: 18/150 (12.0%)
- BNT162b2: 22/154 (14.3%)

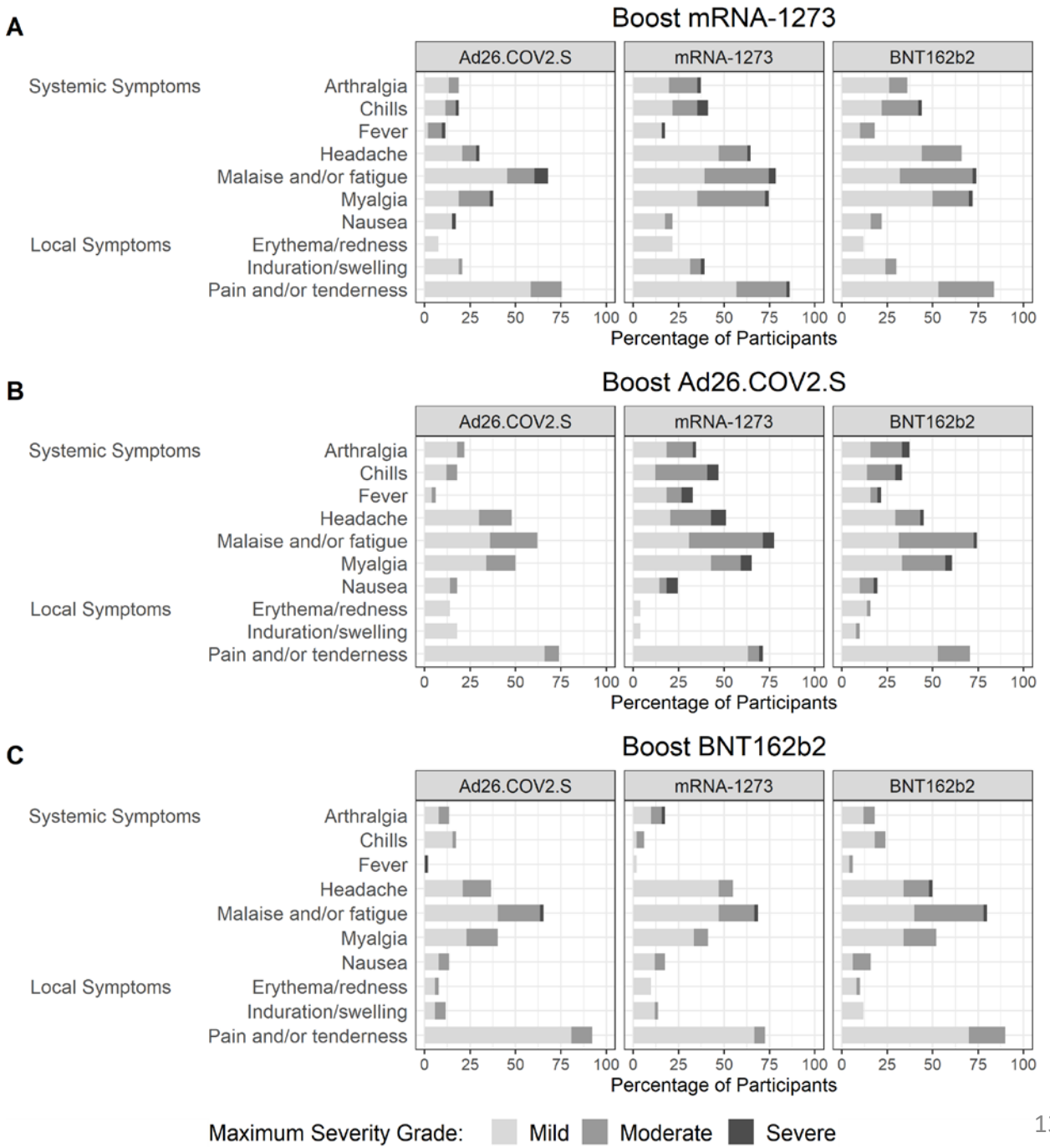
Most related AEs were Grade 1 or 2 severity

Four related Grade 3 AEs:

- Vomiting in one participant - mRNA-1273 booster group
- Vomiting in one participant - Ad26.COV2.S booster group
- Fatigue in one participant - Ad26.COV2.S booster group
- Insomnia in one participant - Ad26.COV2.S booster group

Booster Solicited AEs

Local and Systemic Reactogenicity – Through Day 8



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Limitations -

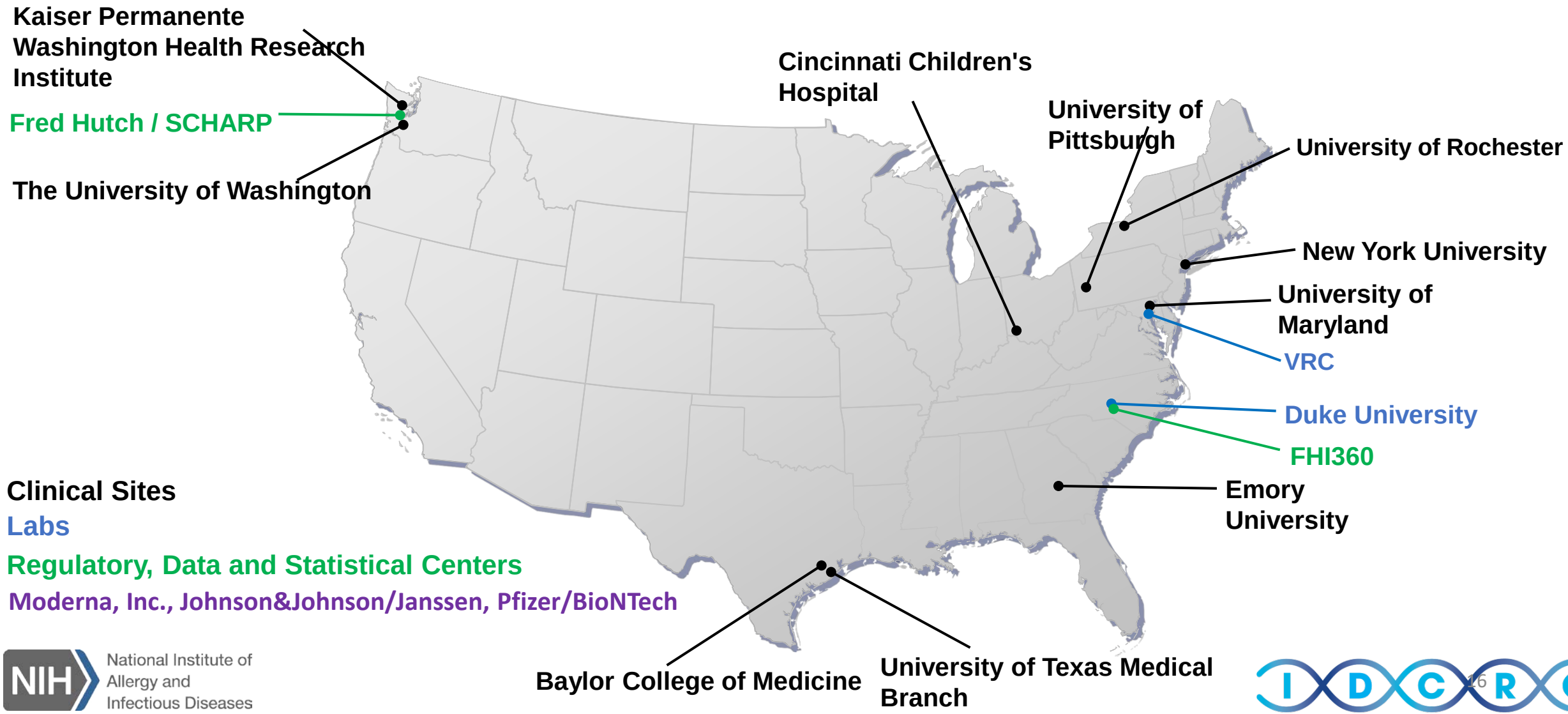
- Non-randomized, open label design
- Study not designed to compare between boosts
  - Didn't control for intervals between primary vaccine and boosts
- Correlates of protection are not completely elucidated
- Correlates for severe disease and death are even less well understood
- This is only antibody data
  - Cellular immune responses are still being analyzed
- These data represent only early timepoints from the trial
  - Vaccines may differ in time to reach peak responses, and may have different durability of the responses

Conclusions -

1. Use of mRNA-1273, Ad26.COV2.S and BNT162b2 as booster vaccines led to anamnestic serologic responses in all 3 EUA-dose vaccine groups
2. For a given primary EUA Covid-19 vaccine, heterologous boosts elicited similar or higher serologic responses as compared to their respective homologous booster responses
3. mRNA vaccines resulted in higher antibody titers in the first 28 days after the boost
4. No safety concerns identified

Preprint: https://www.medrxiv.org/content/10.1101/2021.10.10.21264827v2

The "MixNMatch" Study Team



Questions?