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Safety and Immunogenicity of Mpox Vaccination in Adolescents (DMID 22-0020)

Disclosures or Potential Conflicts of Interest

No disclosures that are directly relevant to this presentation.

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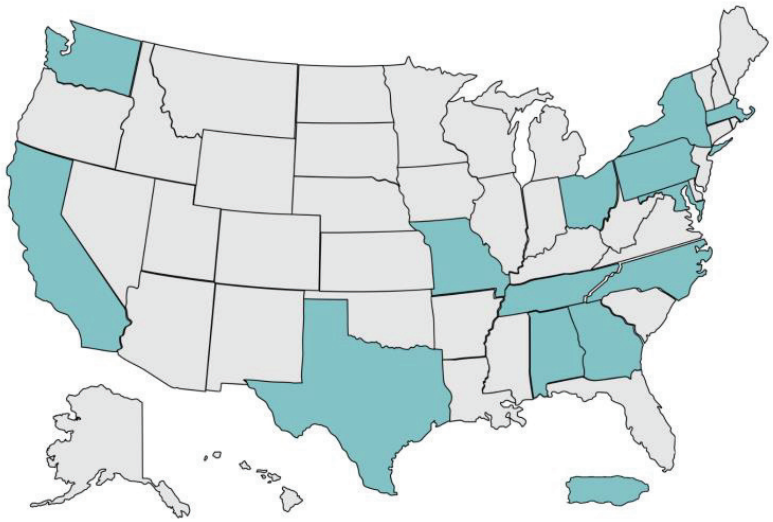

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Phase 2 Randomized, Open-Label, Multisite Trial to Inform Public Health Strategies Involving the Use of MVA-BN Vaccine for Mpox (DoSES)

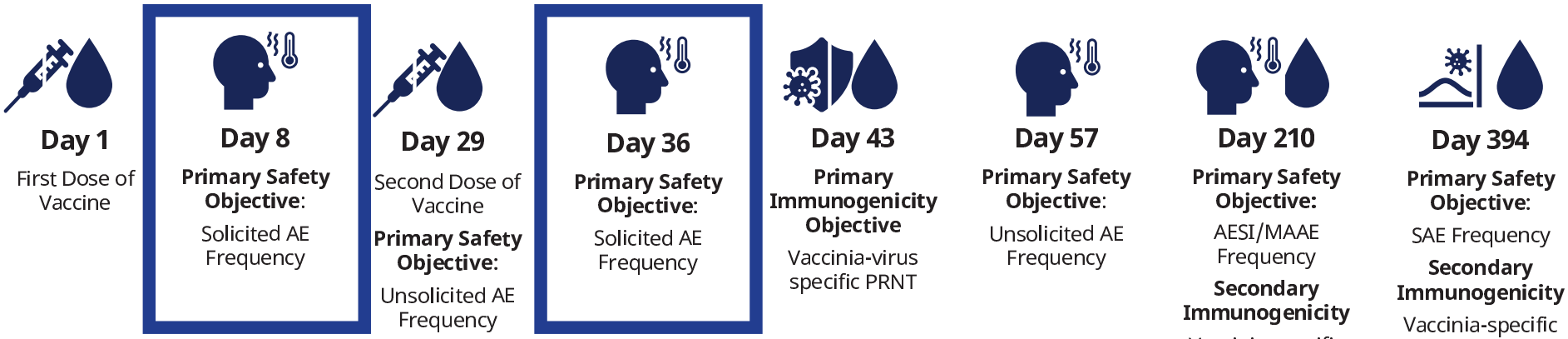
Stage 1 evaluated the FDA-approved, 2 dose subcutaneous (SC) regimen compared with 2 separate intradermal dose-sparing regimens in adults ages 18-50 years.

Stage 2 evaluated the noninferiority of the 2-dose SC regimen in adolescents 12-17 years compared with adults 18-50 years of age.

Methods: Study Design and Objectives

Phase 2, open-label, non-placebo controlled, clinical trial evaluating a 2-dose regimen of $1x10^8$ $TCID_{50}$ MVA-BN administered subcutaneously (SC) on Days 1 and 29 in healthy, vaccinia-naïve adolescents 12-17 years compared to adults 18-50 years of age

- Goal of obtaining licensure of JYNNEOS in adolescents
- Aim to enroll cohort representative of the US population based on 2020 US Census data
- *A priori* target of at least 25% adolescent participants aged 12 to 14 years



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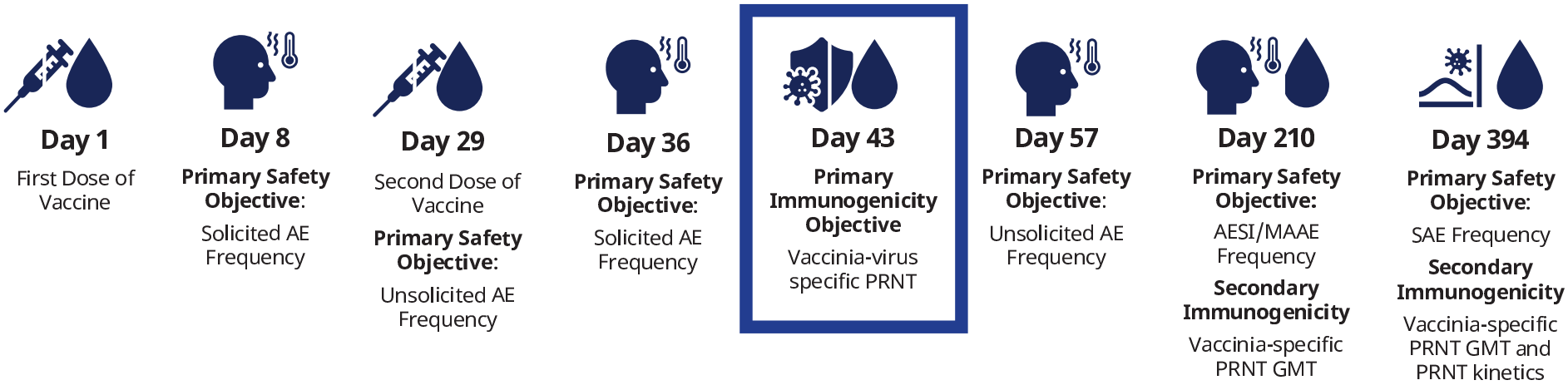

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Day 1

First Dose of Vaccine

Day 8

Primary Safety Objective:

Solicited AE Frequency

Day 29

Second Dose of Vaccine

Primary Safety Objective:

Unsolicited AE Frequency

Day 36

Primary Safety Objective:

Solicited AE Frequency

Day 43

Primary Immunogenicity Objective

Vaccinia-virus specific PRNT

Day 57

Primary Safety Objective:

Unsolicited AE Frequency

Day 210

Primary Safety Objective:

AESI/MAAE Frequency

Secondary Immunogenicity

Vaccinia-specific PRNT GMT

Day 394

Primary Safety Objective:

SAE Frequency

Secondary Immunogenicity

Vaccinia-specific PRNT GMT and PRNT kinetics

Objectives

Assess noninferiority, compared to adults, of a two-dose subcutaneous regimen of 1 x 10^8 $TCID_{50}$ MVA-BN

Safety as assessed by:

- 7-day reactogenicity after each vaccine dose
- 28-day unsolicited AE after each dose
- AE of special interest and medically attended AE through Day 210
- SAE throughout the study period

Secondary objectives included kinetics of the response and rates of seroconversion based on vaccinia-virus specific PRNT

Inclusion Criteria

Adolescent aged 12–17y or adult aged 18-50y

Able and willing to provide consent

In good health per investigator judgment

Willing to follow public health advice regarding avoiding mpox

Females willing to use effective contraception for one month prior to enrollment to Day 57

Well controlled HIV could participate

Exclusion Criteria

Receipt of a licensed or investigational smallpox or mpox vaccine

History of mpox, cowpox or vaccinia infection

Recent contact with mpox

Immunocompromising condition

Recent or current use of immunosuppressive medication

Live viral or COVID-19 vaccination within 1 month of each MVA-BN vaccine dose or any other vaccination within one week of each dose

COVID-19 diagnosis within 1 month prior to dose 1

History of myocarditis or significant heart disease

Significant medical condition per investigator judgment

Scarring or tattoos on arms that would interfere with vaccination site assessment

Results: Study Population

315 adolescents (161[51%] 12-14 years) and
211 adults (135 adults + 76 from Stage 1) participated*

	Adolescent	Adult
Male	160 (51%)	94 (45%)
Age mean (range) years	14.4 (12-17)	34.9 (18-50)
Not Hispanic or Latino	151 (80%)	149 (71%)
Race Asian Black or African American White Multi-Racial	 8 (3%) 31 (10%) 216 (69%) 57 (18%)	 12 (6%) 31 (15%) 145 (69%) 17 (8%)
HIV positive	1 (<1%)	5 (2%)
Received Dose 1	315 (100%)	211 (100%)
Received Dose 2	312 (>99%)	207 (98%)
Completed Primary Endpoint (Day 43)	304 (97%)	208 (99%)

*Adult cohort for primary immunogenicity endpoint included 76 adults enrolled in Stage 1 of the trial who received 1 x10^8 $TCID_{50}$

Results: Safety Summary

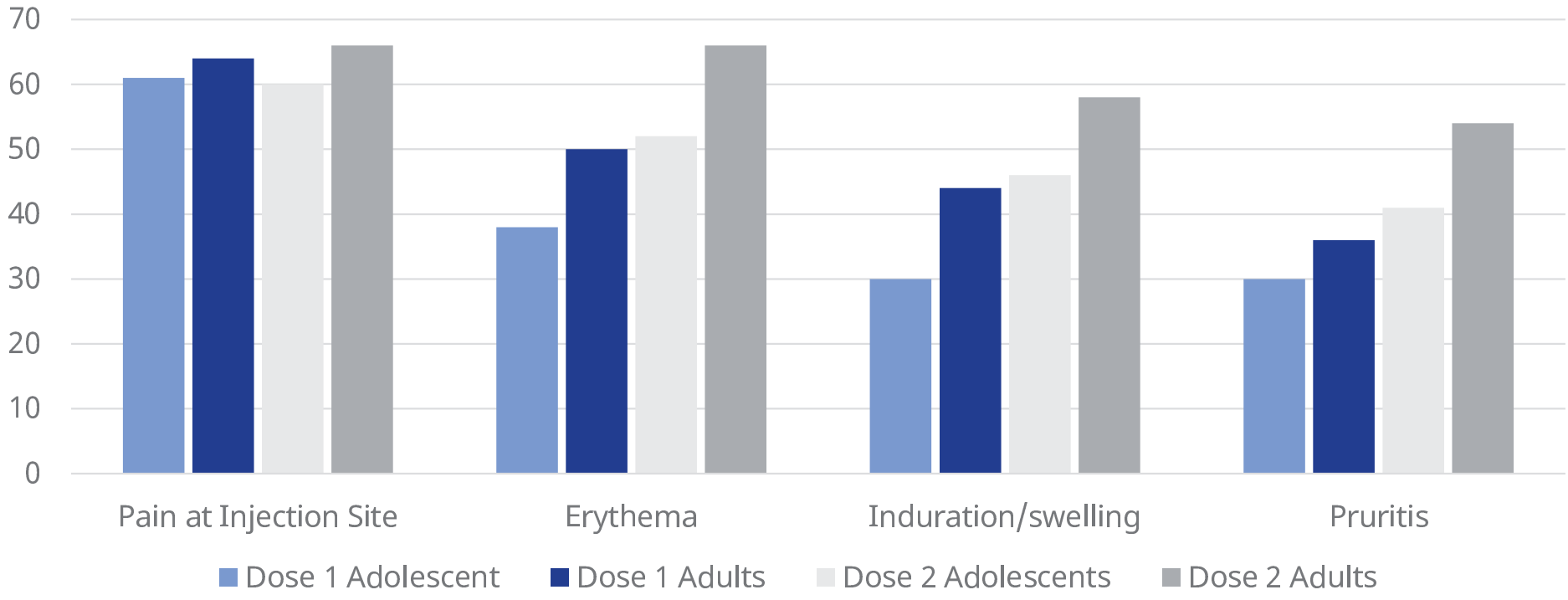
Solicited systemic and local reactions were similar between adolescents and adults

Most common **systemic** reactions were fatigue, headache and myalgia

Most common **local** reactions were pain at the injection site, erythema, and injection site nodules

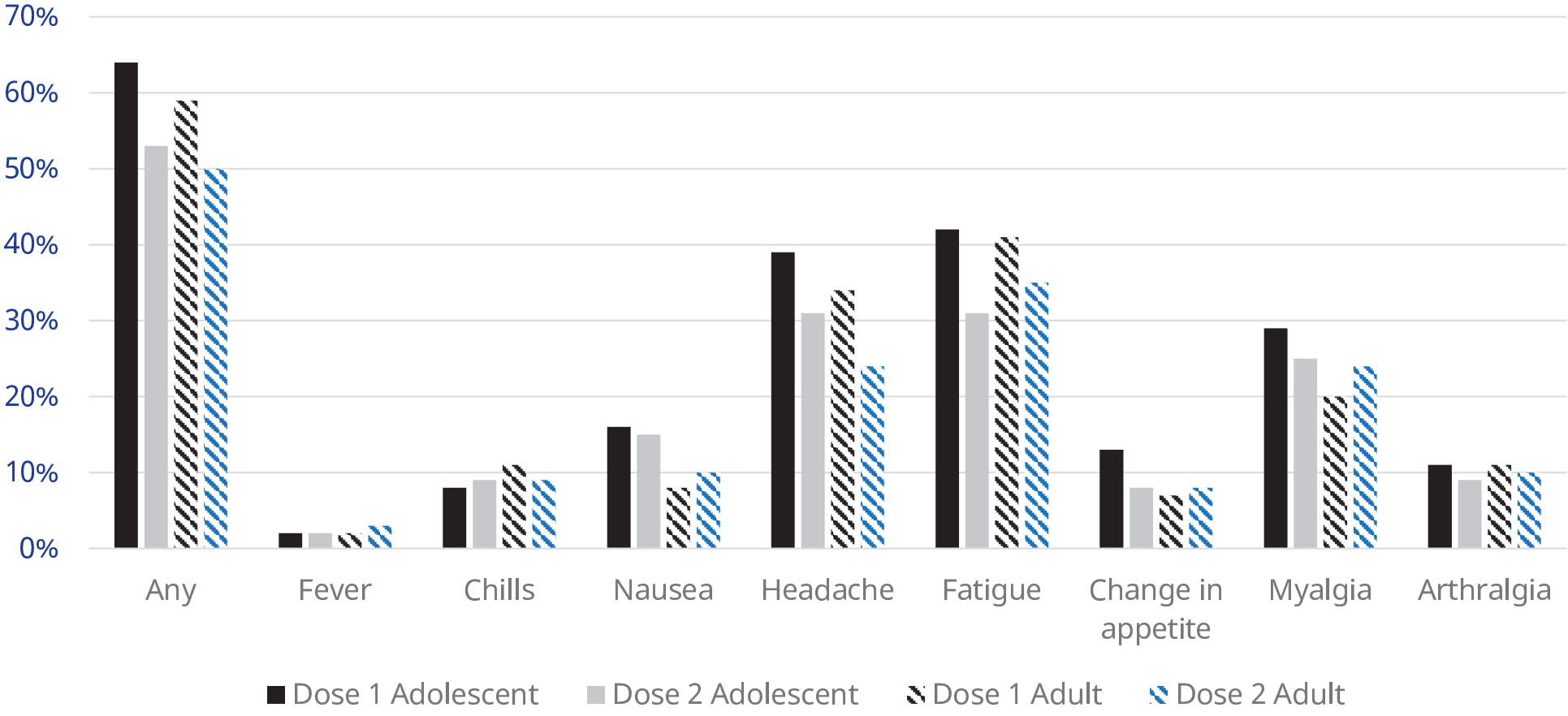
Results: Safety (Local)

Solicited local reactions were similar between adolescents and adults for each dose
In general, erythema, induration and pruritus were more common in both groups after dose 2



Results: Safety (Systemic)

Solicited systemic reactions were similar between adolescents and adults for each dose, and occurred at similar frequencies after dose 1 and dose 2



Severity of Solicited Adverse Events (Reactogenicity)

	Within 7 days of Dose 1	Within 7 days of Dose 2
Adolescents	55% mild 36% moderate 2% severe* (6 participants) *3 fatigue, 1 fever, 1 myalgia, and 1 induration	36% mild 42% moderate 6% severe* (20 participants) * 4 fatigue, 2 nausea, 2 chills, 2 headache, 1 fever, 1 change in appetite, 15 erythema, and 11 induration
Adults	50% mild 31% moderate 3% severe (2 fatigue, 1 arthralgia)	35% mild 37% moderate 19% severe (22 erythema, 12 induration)

Results: Safety (Local Unsolicited Adverse Events)

Injection site nodules: 117 adolescents (37%) reported an injection site nodule that arose, on average, at the beginning of the second week.

- 79 adults (59%) reported nodules
- Rates were similar between younger and older adolescents (40% vs. 34%)

Discoloration: 53 adolescents (17%) vs. 38 (28%)

Results: Safety (Local Reactions)

Injection site discoloration

Median onset: 8 days after vaccination (range 4 – 36 days)

Median duration: 27 days (range 4 – 372 days) after first dose and 16 days (3 - 345 days) after second dose

Injection site nodules

Median onset: 8 days after vaccination (range 2 - 36 days)

Median duration: 22 days (2 – 54 days) after first dose and 11.5 days (3 – 170 days) after second dose

Group	Within 28 Days of Either Dose (n, %)
Nodules	
Adolescents	117 (37%)
Adults	78 (58%)
Discoloration	
Adolescents	53 (17%)
Adults	37 (27%)

Per protocol, second vaccination was given in the opposite arm (unless a tattoo or other reason prevented)

Results: Safety

Dizziness was reported more frequently in adolescents than adults.

- 8 adolescent participants (3%) compared with 0 adult participants reported transient dizziness following vaccination that could not be attributed to another cause.
- No event resulted in syncope or medical attention; 7 occurred within 1 day of vaccination
- Rates were similar to those reported with other adolescent vaccines

Three adolescents and 4 adults received only the first dose of vaccine.

Adolescents (3)	Adults (4)
Arm pain	Anxiety
Post-vaccination response with tachycardia and hypertension that resolved in 2 hours	Failure to meet eligibility criteria (childbearing potential and willing to use contraception)
Acute sinusitis	Injection site nodule
	Vertigo

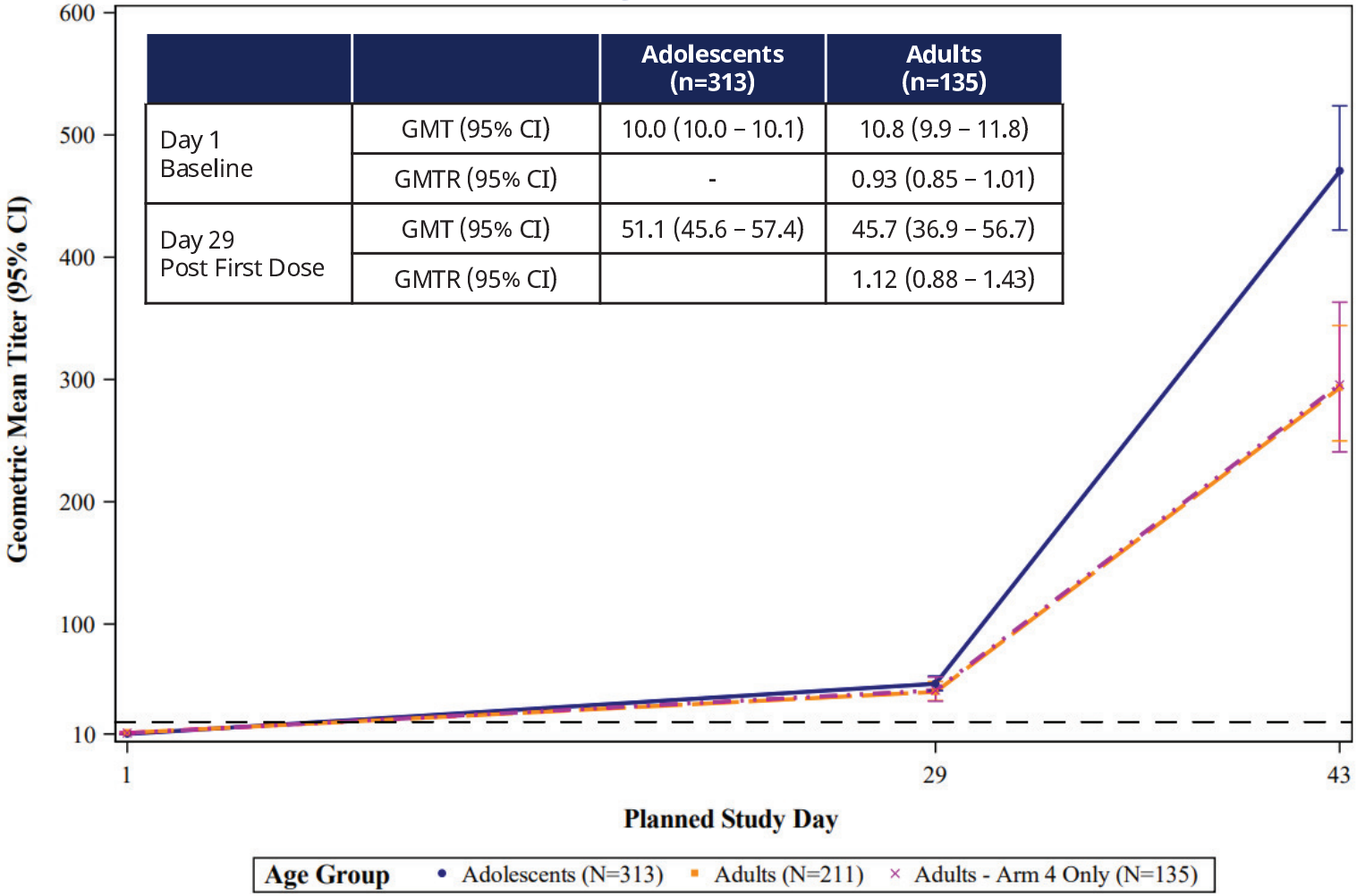
Results: Safety

Two adolescent participants became pregnant during the study.

Both were born without complication and without congenital anomalies

Vaccinia virus (Western Reserve strain) PRNT geometric mean titers elicited by MVA-BN were **higher** in adolescents than adults

		Adolescents (n=313)	Adults (n=135)
Day 1 Baseline	GMT (95% CI)	10.0 (10.0 – 10.1)	10.8 (9.9 – 11.8)
	GMTR (95% CI)	-	0.93 (0.85 – 1.01)
Day 29 Post First Dose	GMT (95% CI)	51.1 (45.6 – 57.4)	45.7 (36.9 – 56.7)
	GMTR (95% CI)		1.12 (0.88 – 1.43)



The adolescent antibody response on Day 43 was non-inferior to adults

304/315 adolescents and 208/211 adults who met criteria for mITT analysis contributed Day 43 samples.

Peak humoral responses (Day 43) after 2 dose regimen in adolescents were non-inferior to adults.

Null hypothesis: Adolescent GMTR lower bound will be ≥0.67.

	Adolescents (n=304)	Adults (n=208)
Geometric Mean Titer (GMT) and 95% CI	470.3 (422.3 – 523.8)	293.2 (249.8 – 344.2)
Geometric Mean Titer Ratio (GMTR) and 95% CI	NA	1.60 (1.32 – 1.95)

Measured by vaccinia virus plaque-reduction neutralization titer (PRNT) assay

p <0.001

Seroconversion in adolescents was similar to adults

		Adolescents (n=313)	Adults (n=211)
Day 29 [a] Pre-Dose 2	GMFR (95% CI)	5.1 (4.5 – 5.7)	4.1 (3.5 – 4.7)
	% Seroconversion	82.6 (77.9 – 86.6)	75.2 (68.8 – 80.9)
Day 43 [b] Post Dose 2	GMFR (95% CI)	46.9 (42.1 – 52.3)	26.7 (22.9 – 31.3)
	% Seroconversion	99.0 (97.1 – 99.8)	97.6 (94.5 – 99.2)
Peak Anytime Post Dose 1[c]	GMFR (95% CI)	45.0 (40.3 – 50.1)	26.9 (23.0 – 31.6)
	% Seroconversion	99.4 (97.7 – 99.9)	97.2 (93.9 – 98.9)

As measured by vaccinia virus plaque-reduction neutralization titer (PRNT) assay;
GMFR=Geometric Mean Fold Rise in antibody compared to pre-dose 1. Seroconversion=% of participants with at least 2-fold rise in antibody titer compared to pre-dose 1.
[a] Adolescents (n=310), Adults (n=210); [b] Adolescents (n=304), Adults (n=208); [c] Adolescents (n=313), Adults (n=211)

Results: MPXV-specific PRNT

MPXV-specific assays are still underway, though no correlate of protection has been defined

Neutralization in the presence of complement appears to be more representative of *in vivo* neutralization.

Testing of various complement sources has led to identification of critical reagents needed for neutralization across both Clade 1 and Clade 2 MPXV

100 paired samples from Stage 1 are being tested against Clade 1 and Clade 2 MPXV in the presence of complement

Limitations

Study population is different compared to the global pediatric population at risk of mpox.

Efforts made to ensure that the population was representative of US population

Ages of volunteers were distributed across the adolescent age group

Conclusions

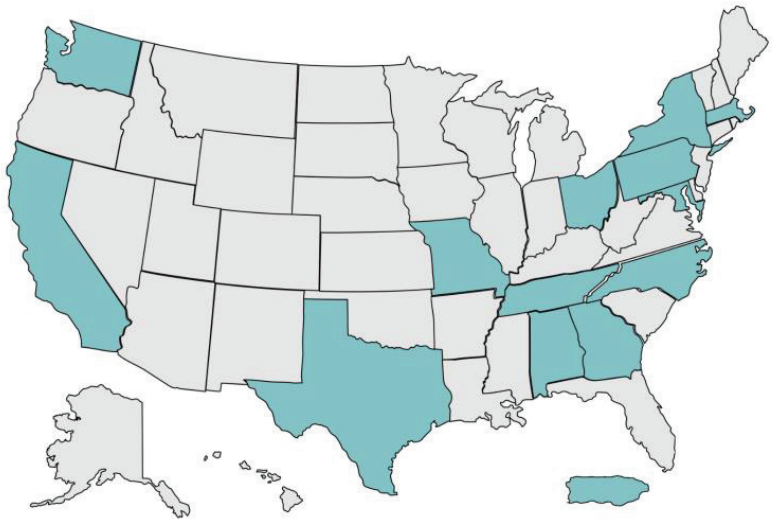
1. The interim data from this Phase 2 clinical trial demonstrate that MVA-BN vaccine is safe and well-tolerated in adolescents aged 12-17 years.

2. The peak GMT met prespecified non-inferiority criteria for adolescents aged 12-17 years as compared to adults aged 18-50 years.

3. These findings are relevant to adolescents in the US and in areas where mpox is endemic, such as the Democratic Republic of the Congo (DRC).

4. Evaluations in younger children are needed to extend protection to those who are most vulnerable, particularly given ongoing transmission among children in the DRC and neighboring countries in Africa.

Acknowledgements



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