mRNA-1273 (Moderna COVID-19 Vaccine) in Individuals 6 - 17 Years of Age

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ACIP

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Approvals, Authorizations and Use of Moderna COVID-19 Vaccine for Children and Adolescents 6-17 Years

- Worldwide approvals / authorizations
  - Adolescents 12-17 in 42 countries (100 µg 2-dose primary series)
  - Children 6-11 in 40 countries (50 µg 2-dose primary series)
- Authorized under EUA in the US on June 17, 2022

Adolescents 12-17 Years

>6.4 Million

Fully vaccinated worldwide

Children 6-11 Years

>300,000

Fully vaccinated worldwide

*Estimated data as of April 15, 2022**

***Data based on estimates from Moderna Bi-Monthly Summary Safety Reports**

EUA for Moderna COVID-19 Vaccine in Children and Adolescents (6 - 17 Years)

Adolescents
12-17 Years

Primary Series
100 µg, 2-Dose

Children
6-11 Years

Primary Series
50 µg, 2-Dose

Indication: Prevention of COVID-19 caused by SARS-CoV-2

Primary Series: 2-dose, intramuscular administration 1 month apart

> 5,800 Children & Adolescents (6-17 Years Old) Received ≥ 1 Dose of mRNA-1273

Study 203 and 204 (Safety Set)

Study	Age Range	Dose Selected	Participants Receiving ≥ 1 Injection		
			mRNA-1273	Placebo	Total
203	12-17 years	100 µg	2,486	1,240	3,726
204	6-11 years	50 µg	3,387	995	4,382
		Total	5,873	2,235	8,108

Median Safety Follow-Up Exceeded FDA Recommendations

Study 203 and 204

Study	Age Range	Part	Dose	mRNA-1273 (N)	Median Follow-Up Post-Dose 2 (Months)
203	12-17 years	Blinded, Randomized	100 µg	2,486	11.1
204	6-11 years	Dose-Ranging	50 µg	380	8.9
			100 µg	371	8.7
		Blinded, Randomized	50 µg	3,007	5.6

1 month = 28 days

Robust Evaluation of Myocarditis and Pericarditis in Clinical Trials of Infants, Toddlers, Children & Adolescents

- Fact Sheets, Investigator Brochures, and Informed Consent Forms updated to increase awareness
- Included as AESIs to enhance detection and support standardized follow-up
- Actively queried symptoms suggestive of myocarditis / pericarditis based on CDC case definition during safety follow-up calls
- Clinical database reviewed for participant-reported symptoms
- Potential events independently adjudicated by Cardiac Event Adjudication Committee (CEAC)

Identification of Potential Subclinical Myocarditis and Pericarditis in Clinical Trials of Infants, Toddlers, Children & Adolescents

- Two methods were used to query the clinical database for potential, subclinical cases of myocarditis
  1. Standard MedDRA queries were applied for myocarditis and pericarditis
  2. Specific algorithm was developed to identify clinical signs and symptoms in the CDC working case definitions for myocarditis and pericarditis
- Ongoing post-authorization safety studies continue to capture myocarditis and pericarditis as AESIs

Primary Effectiveness Objective

Study 203 and 204

Immunogenicity

- GMT of serum antibody and seroresponse rate (day 57) compared to 18-25-year-olds in pivotal efficacy Study 301
  - GMT Ratio lower 95% CI ≥ 0.67 and point estimate ≥ 0.8
    - FDA requested point estimate ≥ 1.0 if doses < 100 µg selected
  - Difference in seroresponse rate lower 95% CI > -10% and point estimate > -5%
- Effectiveness is inferred by immunobridging

Secondary Efficacy Endpoints, COVID-19 Case Definitions

Study 203 and 204

Two COVID-19 Definitions

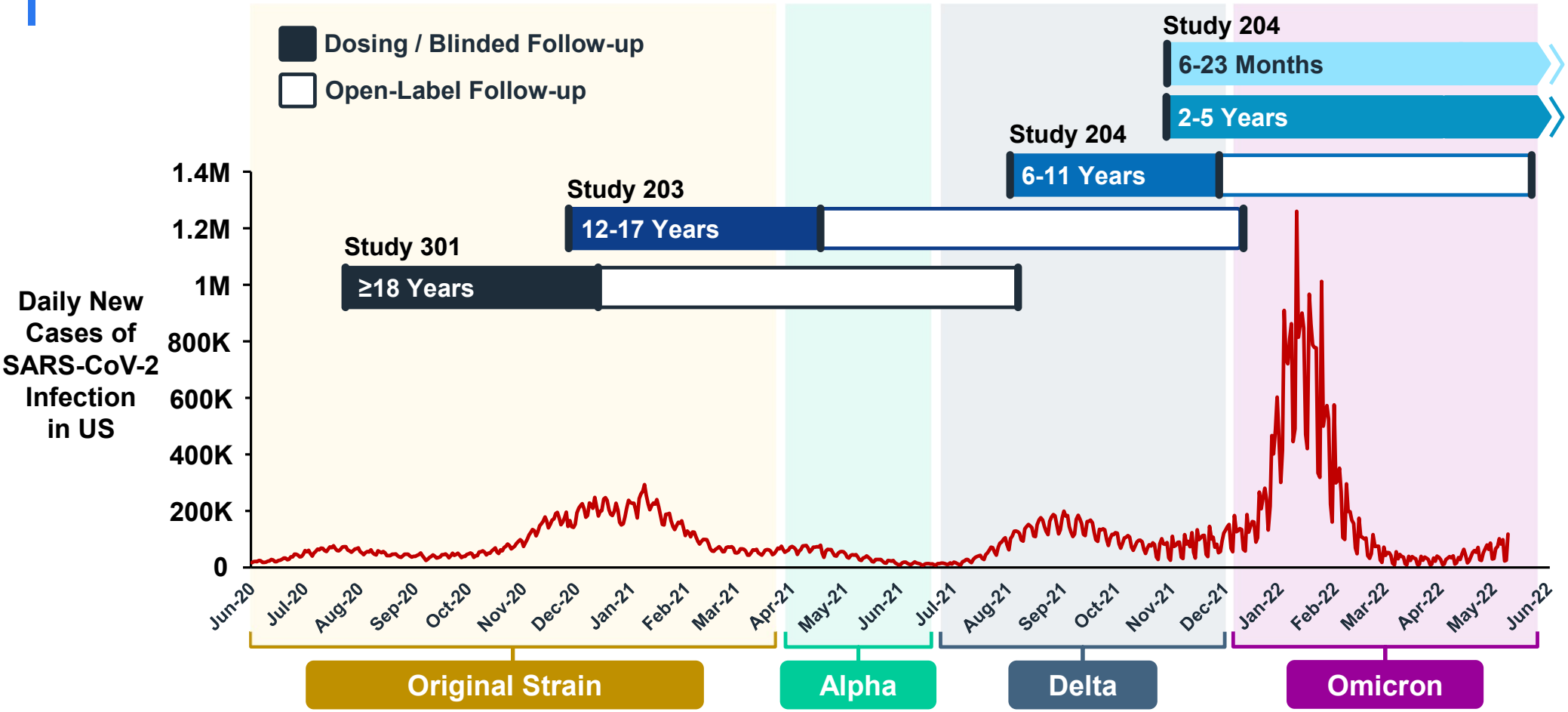
CDC Case Definition

1 systemic symptom or 1 respiratory symptom + a positive RT-PCR

Efficacy (Study 301) Case Definition

2 systemic symptoms or 1 respiratory symptom + a positive RT-PCR

Clinical Studies Conducted During Different Periods of COVID-19 Pandemic

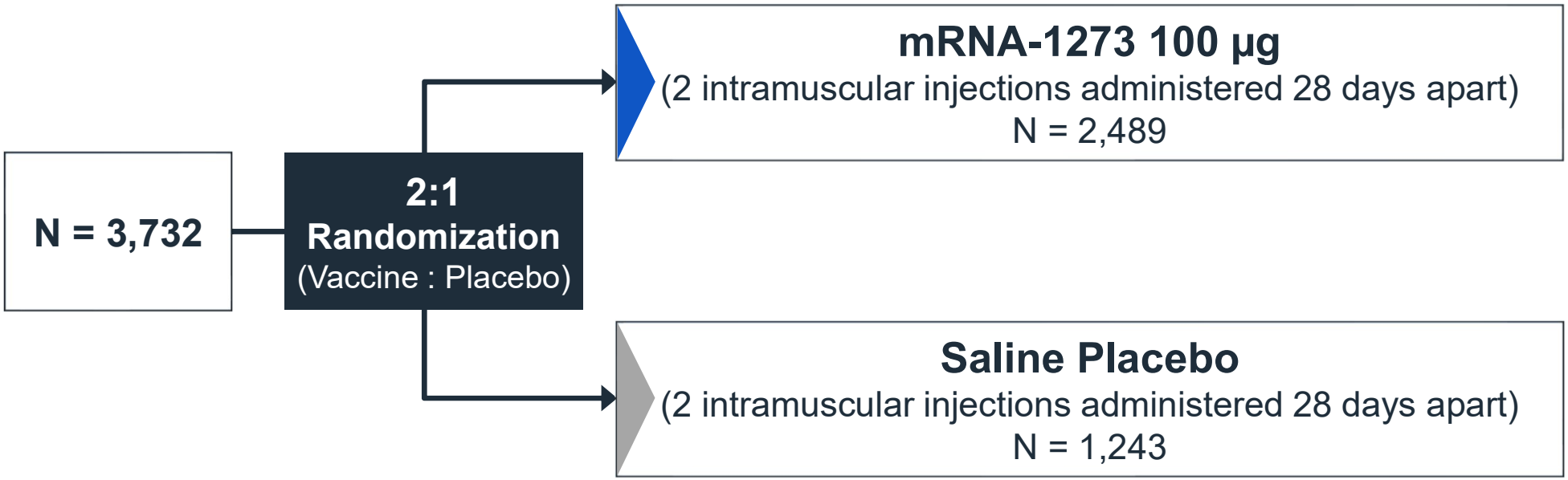


https://covid.cdc.gov/covid-data-tracker/#trends_dailycases

Safety, Immunogenicity, and Efficacy in Adolescents 12 - 17 Years of Age

Pivotal, Randomized, Placebo-Controlled Evaluation of Safety, Immunogenicity, and Efficacy

Study 203: Adolescents (12-17 Years)



- **Planned follow-up:** 12-months after last dose

Ali et al., *NEJM* 2021

Demographics

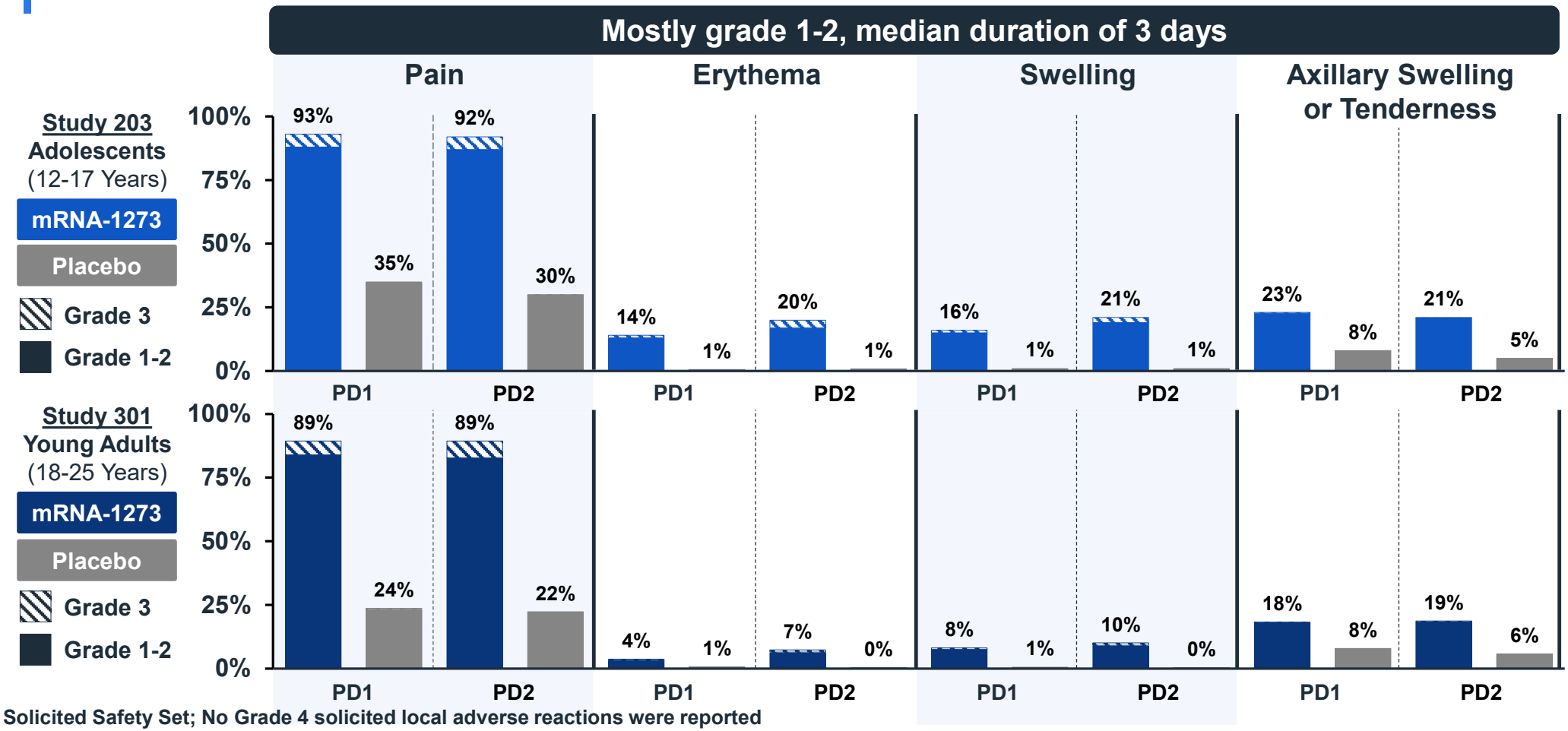
Study 203: Adolescents (12-17 Years), Safety Set

		mRNA-1273 N = 2,486	Placebo N = 1,240
Age (years)	Mean	14.3	14.2
	12-15	74%	75%
	16-18	26%	25%
Gender	Female	48%	49%
Race	White	84%	84%
	Black or African American	3%	3%
	Asian	6%	6%
	American Indian or Alaska Native	0.5%	0.6%
	Multiracial	5%	4%
Ethnicity	Hispanic or Latino	11%	12%
	Not Hispanic or Latino	88%	87%

Ali et al., *NEJM* 2021

Solicited Local Adverse Reactions within 7 Days After Dose 1 & 2

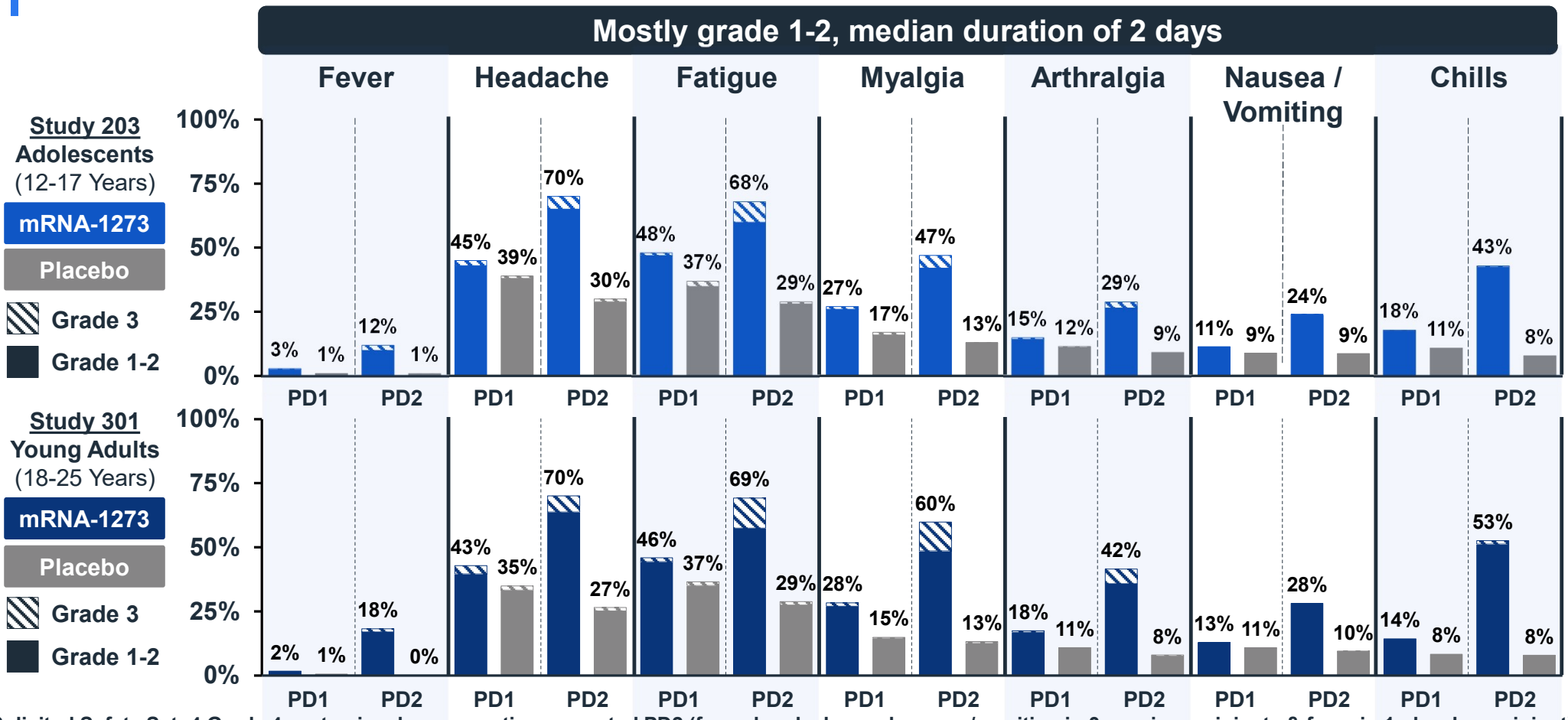
Study 203: Adolescents (12-17 Years) vs Study 301: Young Adults (18-25 Years)



Solicited Safety Set; No Grade 4 solicited local adverse reactions were reported

Solicited Systemic Adverse Reactions within 7 Days After Dose 1 & 2

Study 203: Adolescents (12-17 Years) vs Study 301: Young Adults (18-25 Years)



Solicited Safety Set; 4 Grade 4 systemic adverse reactions reported PD2 (fever, headache, and nausea/vomiting in 3 vaccine recipients & fever in 1 placebo recipient)

Unsolicited Adverse Events

Study 203: Adolescents (12-17 Years), Safety Set, Up to 28 Days After Any Injection

2:1 Randomization (mRNA-1273:Placebo)	mRNA-1273 N = 2,486		Placebo N = 1,240	
	Any AE	Related to Vaccination	Any AE	Related to Vaccination
All	21%	13%	16%	6%
SAE	<0.1%	0	<0.1%	0
Fatal	0	0	0	0
Medically Attended AEs	6.3%	0.8%	6.5%	0.4%
Leading to Discontinuation - Vaccine	0	0	0	0
Leading to Discontinuation - Study	<0.1%	0	0	0
Severe	0.2%	0	<0.1%	0
AESI of MIS-C	0	0	0	0

2 AESIs retrospectively identified at 31 Jan 2022 data cut following 27 Jul 2021 protocol amendment

- Events were appendicitis (N=1) and injection site hypersensitivity (N=1)

Serious Adverse Event (SAE), Multisystem Inflammatory Syndrome in Children (MIS-C), Adverse Event of Special Interest (AESI)

Long-Term Safety – 11.1 Months Median Duration of Follow-Up After Dose 2

Study 203: Adolescents (12-17 Years), Safety Set

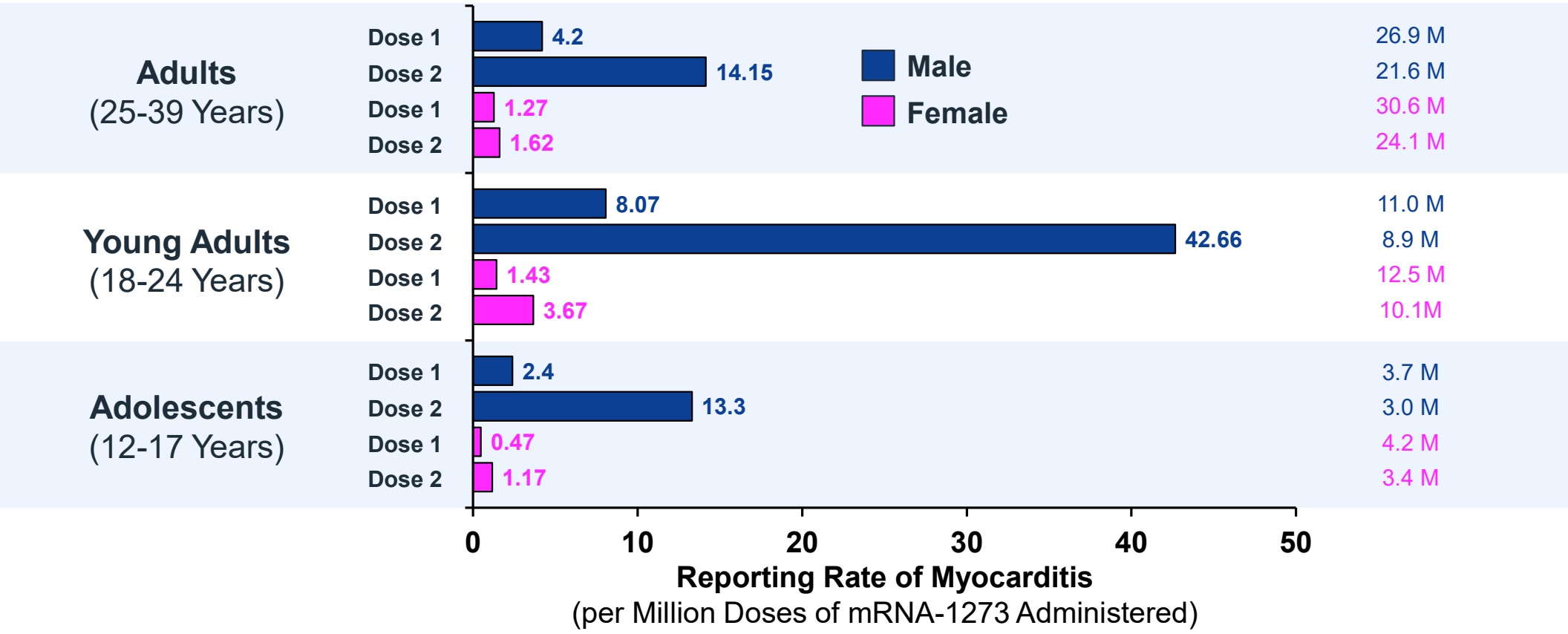
	mRNA-1273 N = 2,486			
	Any AE		Related to Vaccination	
	n	%	n	%
SAE	21	0.8%	0	-
Fatal	0	-	0	-
Medically Attended AEs	980	39.4%	25	1.0%
Leading to Discontinuation - Vaccine	3	0.1%	1	<0.1%
Leading to Discontinuation - Study	0	-	0	-
AESI – Any	13	0.5%	1	<0.1%
AESI of MIS-C	0	-	0	-
AESI of Other	13	0.5%	1	<0.1%

1 SAE in mRNA-1273 participant, reported within 28 days, identified at 31 Jan 2022 data cut

Serious Adverse Event (SAE), Multisystem Inflammatory Syndrome in Children (MIS-C), Adverse Event of Special Interest (AESI)

Myocarditis Reporting Rates with mRNA-1273 in Post Licensure Follow-up

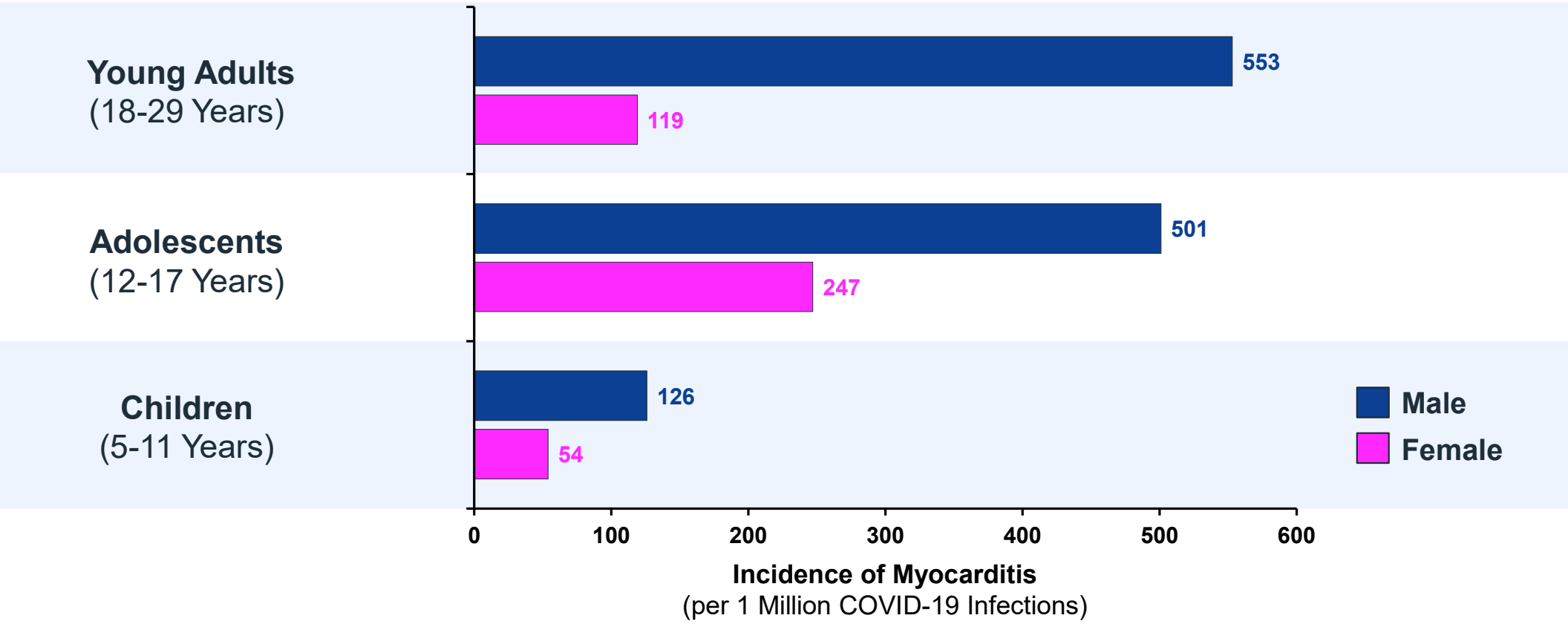
Moderna Global Safety Database (as of April 15, 2022)



*Numbers vaccinated estimated from April 15, 2022 Moderna Bi-Monthly Summary Safety Reports

Myocarditis Reporting Rates Associated with SARS-CoV-2 Infections

PCORnet United States, Jan 2021 – Jan 2022



Block, J. P. et al. Cardiac Complications After SARS-CoV-2 Infection and mRNA COVID-19 Vaccination — PCORnet, United States, January 2021–January 2022. Mmwr Morbidity Mortal Wkly Rep 71, (2022).

Co-Primary Immunogenicity Objectives of GMT Ratio and Seroresponse Rate were Met

Study 203: Adolescents (12-17 Years), Per Protocol Immunogenicity Subset

Day 57 Analysis PsVNA	Study 203 **Adolescents** (12-17 Years) **mRNA-1273 (100 µg)** N = 340	Study 301 **Young Adults** (18-25 Years) **mRNA-1273 (100 µg)** N = 296
GMT (Geometric Mean Titer) 95% CI	**1401.7** (1276.3, 1539.4)	**1301.3** (1177.0, 1438.8)
GMT Ratio (Study 203 vs 301) 95% CI	**1.1** (0.9, 1.2)	
Seroresponse, n/N (%) 95% CI	**336 (98.8%)** (97.0, 99.7)	**292 (98.6%)** (96.6, 99.6)
Difference (Study 203 vs 301) 95% CI	**0.2%** (-1.8, 2.4)	

Success Criteria Met

GMT Ratio: Lower 95% CI ≥ 0.67 & Point Estimate ≥ 0.8

Difference in Seroresponse Rate: 95% CI > -10% & Point Estimate > -5%

Vaccine Efficacy in Blinded Phase (through May 8, 2021)

Study 203: Adolescents (12-17 Years), Per Protocol Set, COVID-19 Cases Starting 14 Days After Dose 2

	mRNA-1273 100 µg	Placebo
CDC case definition of COVID-19		
Cases, n/N (%)	1 / 2,139 (<0.1)	7 / 1,042 (0.7)
Incidence rate per 1000 person-years (95% CI)	1.9 (0.0, 10.8)	29.0 (11.7, 59.7)
VE (%) based on incidence rate (95% CI)	**93.3% (47.9, 99.9)**	
301 case definition of COVID-19		
Cases, n/N (%)	0 / 2,139 (0)	4 / 1,042 (0.4)
Incidence rate per 1000 person-years (95% CI)	0 (NE, 7.1)	16.5 (4.5, 42.3)
VE (%) based on incidence rate (95% CI)	**100% (28.9, NE)**	

CDC case definition: 1 systemic or 1 respiratory symptom + positive RT-PCR
301 case definition: 2 systemic or 1 respiratory symptom + positive RT-PCR

Ali et al, *NEJM*, 2021

Study 204: Safety, Immunogenicity, and Efficacy of mRNA-1273 in Children, 6 - 11 Years of Age

Dose Selection (Part 1) Followed by Randomized, Placebo-Controlled Study (Part 2)

Study 204: Children (6-11 Years)

Part 1

Open-Label, Dose Selection

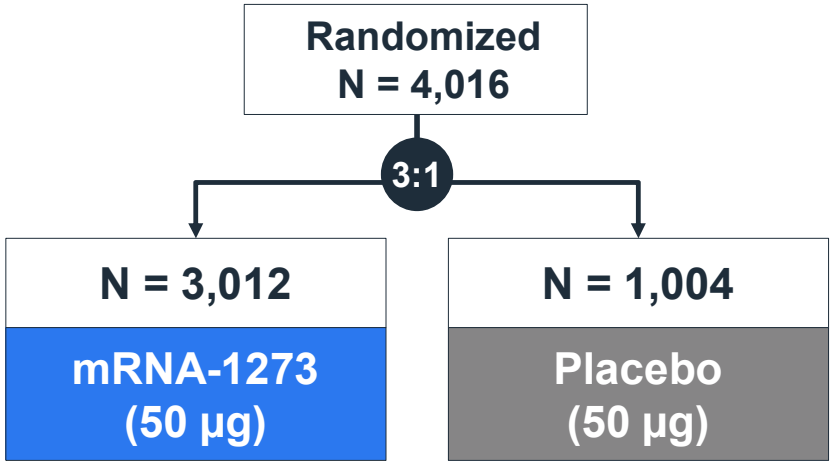
N = 371	N = 380
mRNA-1273 (100 µg)	mRNA-1273 (50 µg)

Dose Selected

- Showed acceptable tolerability profile
- High likelihood of meeting immunogenicity criteria
- External DSMB agreed with 50 µg dose

Part 2

Randomized, Placebo-Controlled



- Randomized 3:1 (mRNA-1273:Placebo)
- 12-month planned follow-up after last dose

Demographics

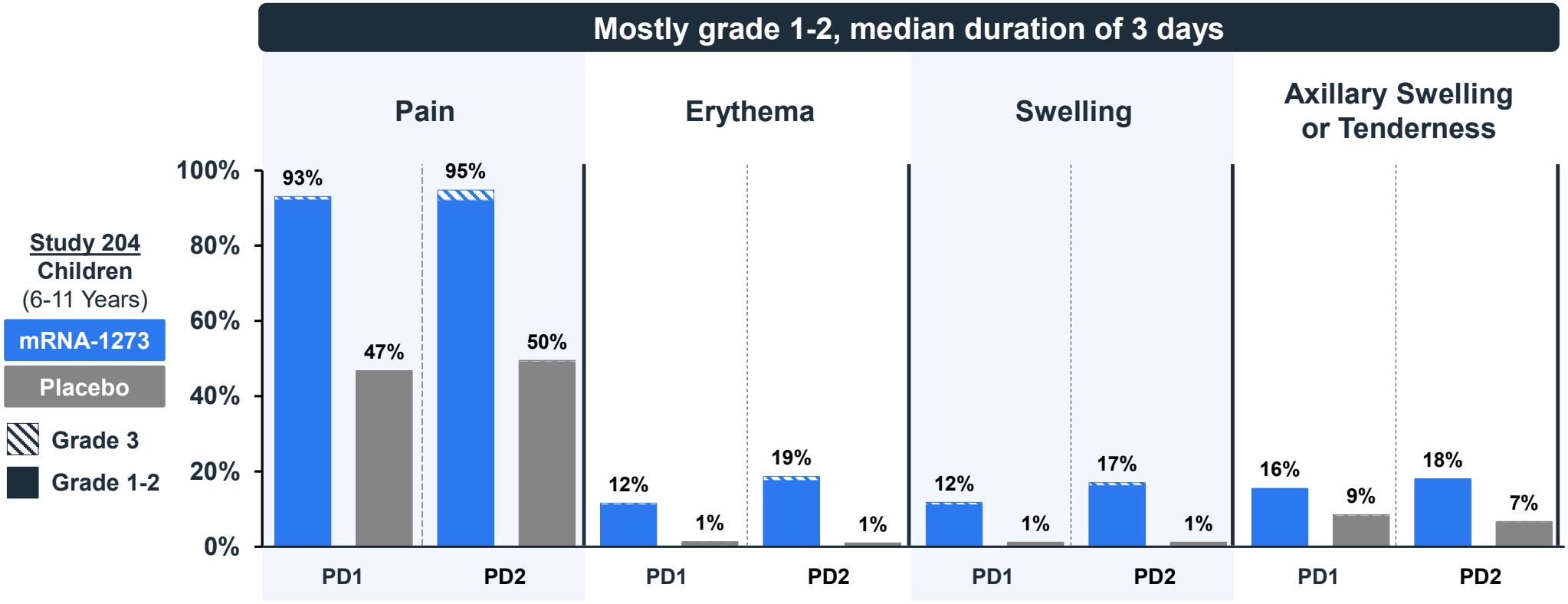
Study 204 (Part 2): Children (6-11 Years), Safety Set

		mRNA-1273 (50 µg) N = 3,007	Placebo N = 995
Age	Mean (Years)	8.5	8.5
	6-8 Years	50%	49%
	9-11 Years	50%	51%
Gender	Female	48%	52%
Race	White	65%	67%
	Black or African American	10%	9%
	Asian	10%	10%
	American Indian or Alaska Native	< 1%	< 1%
	Multiracial	11%	10%
Ethnicity	Hispanic or Latino	19%	18%
	Not Hispanic or Latino	80%	81%

Creech et al., *NEJM*, 2022

Solicited Local Reactions within 7 Days After Dose 1 & 2

Study 204: Children (6-11 Years)

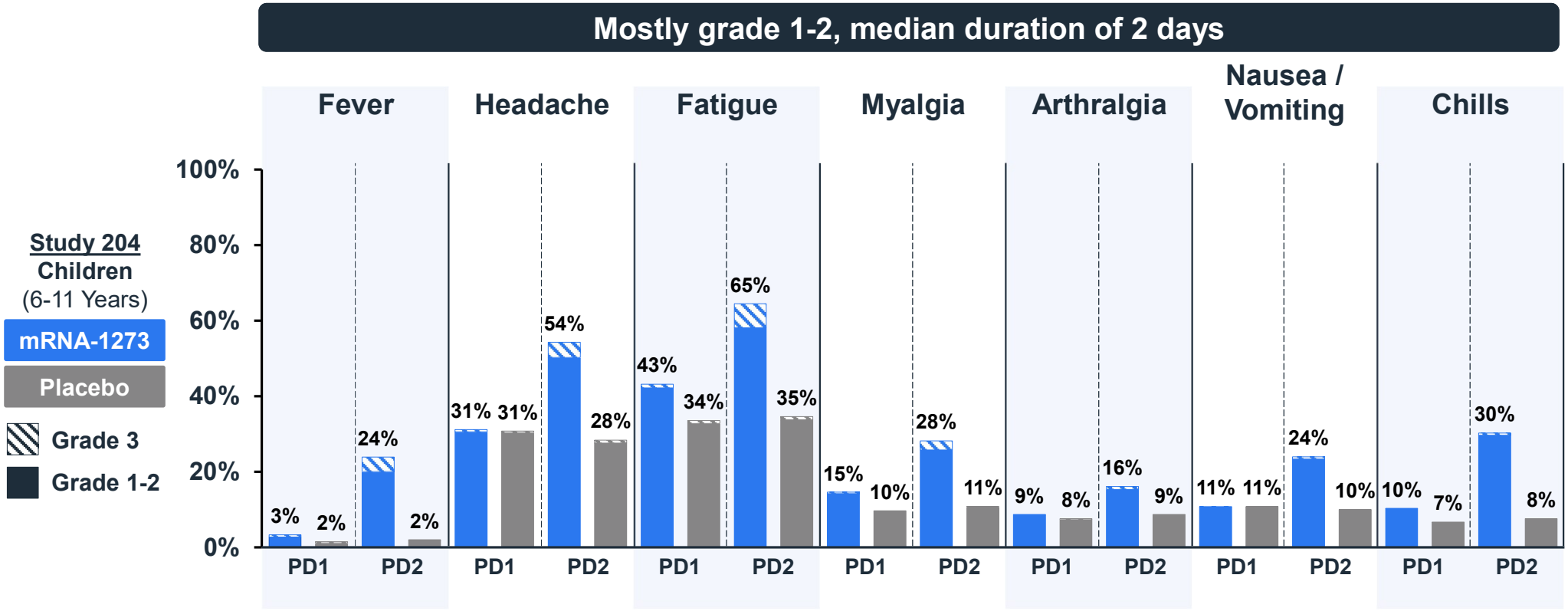


Solicited Safety Set; SARS-CoV2 negative at baseline; No Grade 4 local reactions reported

Creech et al., *NEJM*, 2022

Solicited Systemic Reactions within 7 Days After Dose 1 & 2

Study 204: Children (6-11 Years)



Solicited Safety Set; SARS-CoV2 negative at baseline; No Grade 4 systemic reactions reported

Creech et al., *NEJM*, 2022

Unsolicited Adverse Events

Study 204: Children (6-11 Years), Safety Set (Part 2), Up to 28 Days After Any Injection

3:1 Randomization (mRNA-1273:Placebo)	mRNA-1273 N = 3,007		Placebo N = 995	
	Any AE	Related to Vaccination	Any AE	Related to Vaccination
All	30%	11%	25%	5%
SAE	<0.1%	0	0.2%	0
Fatal	0	0	0	0
Medically Attended AEs	13%	1%	14%	0.4%
Leading to Discontinuation - Vaccine	<0.1%	0	0	0
Leading to Discontinuation - Study	<0.1%	0	0	0
Severe	0.4%	0.3%	0.2%	0.1%
AESI – Any	<0.1%	0	0.2%	0
AESI of MIS-C	0	0	0	0
AESI of Myocarditis/Pericarditis	0	0	0	0

Serious Adverse Event (SAE), Multisystem Inflammatory Syndrome in Children (MIS-C), Adverse Event of Special Interest (AESI)

Long-Term Safety – 5.6 Months Median Duration of Follow-Up After Dose 2

Study 204: Children (6-11 Years), Safety Set (Part 2)

	mRNA-1273 N = 3,007			
	Any AE		Related to Vaccination	
	n	%	n	%
All	1517	50%	364	12%
SAE	15	0.5%	0*	0
Fatal	0	0	0	0
Medically Attended AEs	1028	34%	38	1.3%
Leading to Discontinuation - Vaccine	3	<0.1%	1	<0.1%
Leading to Discontinuation - Study	1	<0.1%	0	0
Severe	23	0.8%	11	0.4%
AESI – Any	12	0.4%	1	<0.1%
AESI of MIS-C	0	0	0	0
AESI of Myocarditis/Pericarditis	0	0	0	0

1 related SAE of ileus reported in participant from placebo cross-over group with a complex GI medical history

Serious Adverse Event (SAE), Multisystem Inflammatory Syndrome in Children (MIS-C), Adverse Event of Special Interest (AESI)

Prespecified Co-Primary Immunogenicity Objectives of GMT Ratio and Seroresponse Were Met

Study 204 (Part 2): Children (6-11 Years), Per Protocol Immunogenicity Subset

Day 57 Analysis, Part 2 PsVNA	Study 204 **Children** (6-11 Years) **mRNA-1273 (50 µg)** N = 320	Study 301 **Young Adults** (18-25 Years) **mRNA-1273 (100 µg)** N = 295
GMT (Geometric Mean Titer) 95% CI	**1610** (1457, 1780)	**1300** (1171, 1443)
GMT Ratio (Study 204 vs. 301) 95% CI	**1.2** (1.1, 1.4)	
Seroresponse, n/N (%) 95% CI	**313/316 (99.1%)** (97.3, 99.8)	**292/295 (99.0%)** (97.1, 99.8)
Difference (Study 204 vs. 301) 95% CI	**0.1%** (-1.9, 2.1)	

Success Criteria Met

GMT Ratio: Lower 95% CI ≥ 0.67 & Point Estimate ≥ 0.8

Difference in Seroresponse Rate: 95% CI > -10% & Point Estimate > -5%

Availability of an EUA Vaccine for 6-11 Year Age Group Limited Efficacy Follow-up During Blinded Period

- Participants unblinded to allow placebo recipients to either:
  - Cross-over to receive mRNA-1273 and remain in study
  - Withdraw from study to receive authorized vaccine
- Loss of placebo comparator group limited efficacy follow-up during blinded period (1.8 months median post-dose 2)
- Analysis conducted in mITT1 using cases accrued 14 days post-dose 1

Efficacy of mRNA-1273 During Delta Period

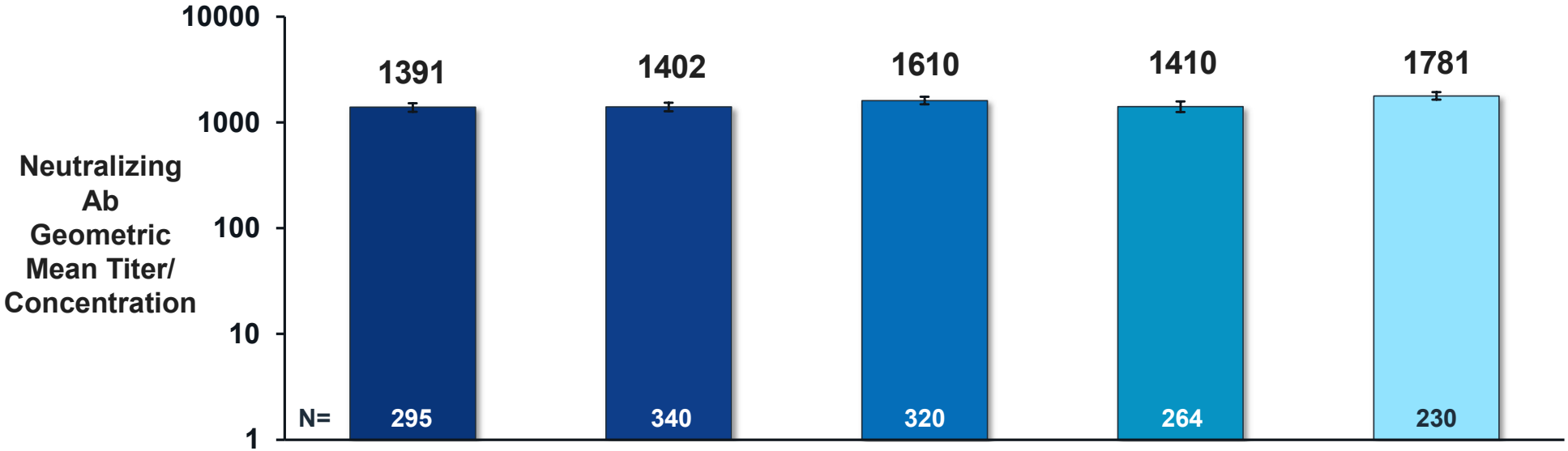
Study 204 (Part 2): Children (6-11 Years), mITT1 Starting 14 Days After Dose 1

	mRNA-1273 50 µg	Placebo
CDC case definition of COVID-19		
Cases, n/N (%)	7 / 2,680 (0.3%)	18 / 875 (2.1%)
Incidence rate per 1000 person-years (95% CI)	14 (6, 29)	117 (69, 185)
VE (%) based on incidence rate (95% CI)	**88.0%** (70.0, 95.8)	
301 case definition of COVID-19		
Cases, n/N (%)	4 / 2,681 (0.1%)	15 / 877 (1.7%)
Incidence rate per 1000 person-years (95% CI)	8 (2, 20)	97 (54, 160)
VE (%) based on incidence rate (95% CI)	**91.8%** (74.2, 98.0)	

CDC case definition: 1 systemic or 1 respiratory symptom + positive RT-PCR
301 case definition: 2 systemic or 1 respiratory symptom + positive RT-PCR

Creech et al., *NEJM*, 2022

Immunogenicity of mRNA-1273 1 Month After a 2-Dose Primary Series, Consistent Across All Age Groups



	Study 301 Young Adults (18-25 Years)	Study 203 Adolescents (12-17 Years)	Study 204 Children (6-11 Years)	Study 204 Young Children (2-5 Years)	Study 204 Infants/Toddlers (6-23 Months)
Dose	100 µg	100 µg	50 µg	25 µg	25 µg
Geometric Mean Ratio (vs Young Adults)		1.1	1.2	1.01	1.28

Summary of Moderna COVID-19 Vaccine in Children & Adolescents, 6-17 Years of Age

Safety (Primary Objective)	▪ mRNA-1273 generally well tolerated ▪ Safety profile consistent with young adults ▪ No new safety concerns have been identified
Immunogenicity (Primary Objective)	▪ Designed to meet FDA recommendations for Emergency Use Authorization for COVID-19 vaccines ▪ Co-primary immunogenicity objectives met for 2-dose primary series
Efficacy (Secondary Objective)	▪ Evidence of vaccine efficacy against COVID-19 with mRNA-1273 ▪ 88% - 100% in children and adolescents (6-17 years)*

*Vaccine efficacy for Children (6-11 Years) based on mITT1 population

THANK YOU to Our Study Collaborators, Investigators, and Participants

- All investigators
- Study site personnel
- BARDA
- NIH & COV-PN
- Most importantly, the infants, toddlers, children, and adolescents who participated in these trials & their families