Overview of BLA for Use of Moderna's COVID-19 Vaccine (Spikevax) in Individuals ≥18 Years of Age

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Outline of Presentation

BLA Overview

- Brief review of:
  - Contents of the BLA
  - Indication
  - Dosage & Administration
- Phase 3 safety data
- Phase 3 efficacy data
- Summary

Q & A

Data Included in BLA Approved by FDA, 1/31/22

- Primary series administration of SPIKEVAX to individuals ≥18 years of age
- Median months of follow-up:
  - Blinded phase - 5.3 months
  - Blinded + open label phases - 7.6 months
- BLA does not include:
  - Indication for use of 100 μg 3rd dose in immunocompromised (EUA approved Aug 13, 2021)
  - Indication for 50 μg booster dose (EUA approved Oct 18, 2021)
  - Data on Omicron variant

BLA - Proposed Indication/Dosage & Administration

- Indication
  - SPIKEVAX is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥18 years of age

- Dosage & Administration
  - IM injection of a series of two 0.5 mL doses each 1 month apart (100 μg dose)

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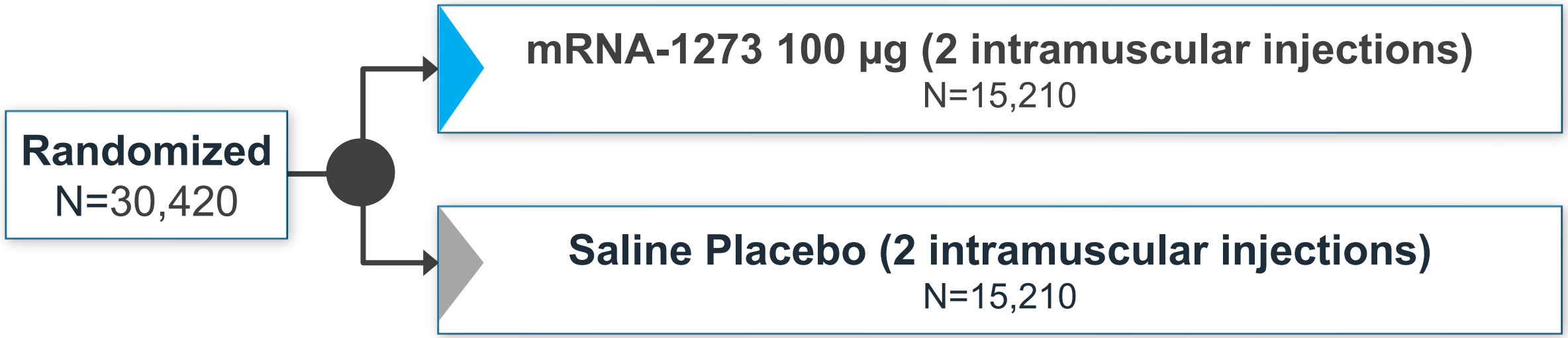
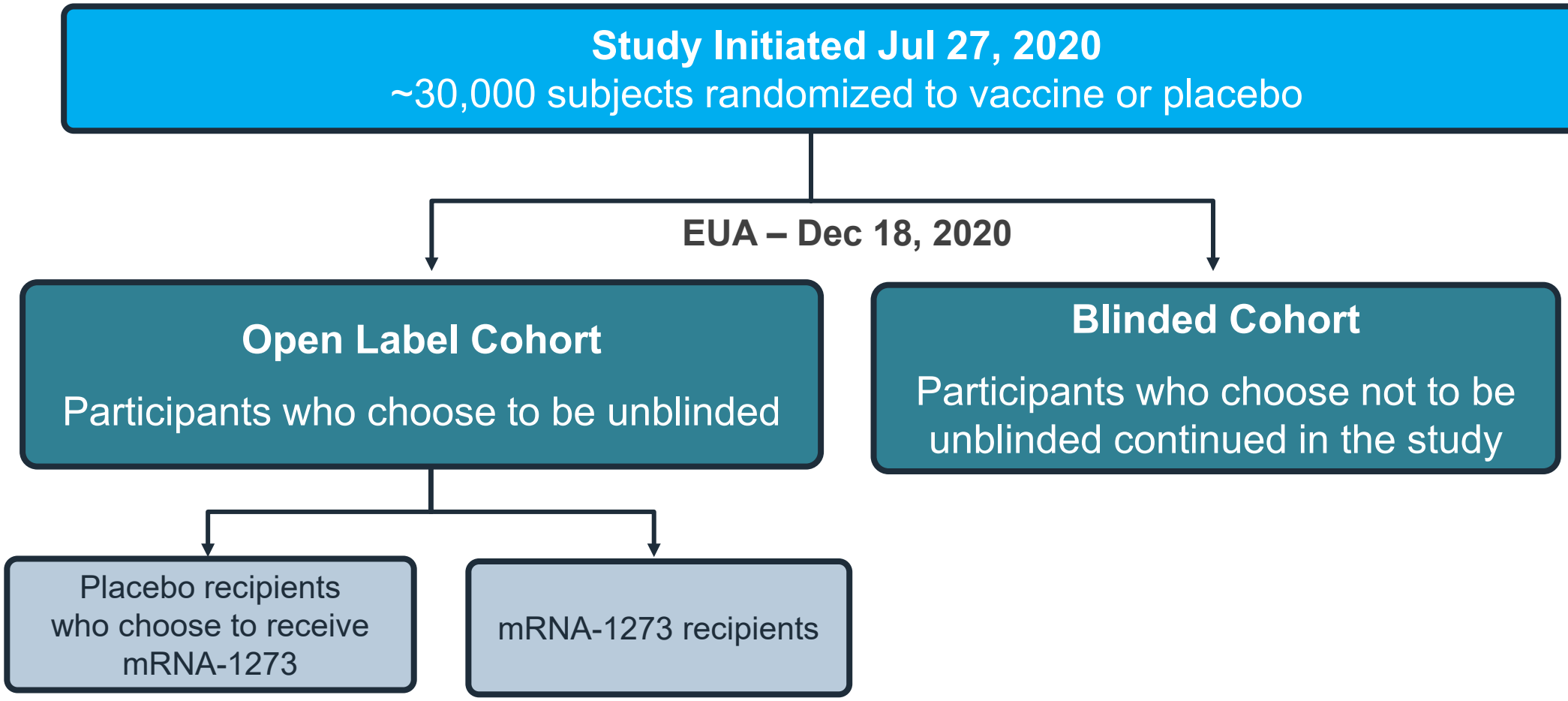
Study 301 – Large Scale Safety & Efficacy Trial

Study 301: Pivotal, Randomized, Placebo-Controlled Evaluation of Efficacy and Safety

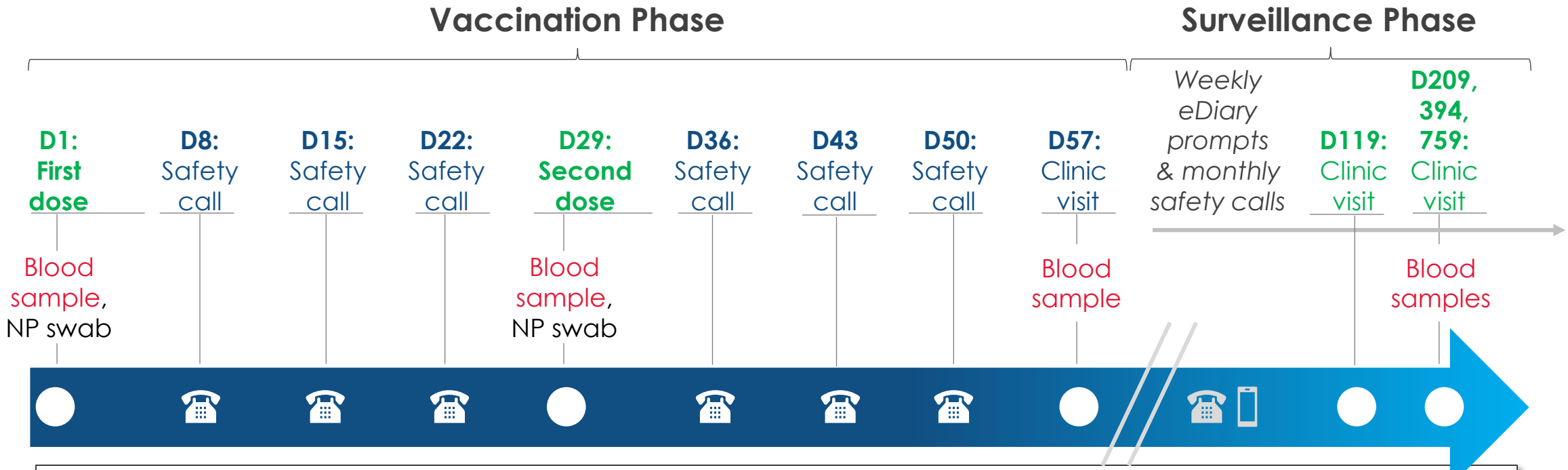


Design of COVE Pivotal Efficacy Trial (P301) Over Time



- **All participants continued on original study schedule of events**
- **Median of 5.3 months of blinded follow-up in BLA**

Study 301: Scheduled Visits and Safety Calls



eDiary captures solicited local and systemic adverse reactions in all participants
SAEs and MAAEs captured throughout the study
COVID-19 active surveillance throughout the study
Daily telemedicine visits for participants with COVID-19

Study 301: Representation of Participants with Risk Factors

Full Analysis Set

	mRNA-1273 N=15,180		Placebo N=15,166	
	n	%	n	%
Age and health risk for severe COVID-19				
18-64 without comorbid conditions	8,888	**59%**	8,882	**59%**
18-64 with comorbid conditions	2,530	**17%**	2,535	**17%**
≥ 65 with and without comorbid conditions	3,762	**25%**	3,749	**25%**

Comorbid conditions included chronic lung disease or moderate to severe asthma, significant cardiac disease, severe obesity, diabetes, liver disease, stable HIV infection

Race/Ethnicity Enrollment Distribution Compared to US Population

Full Analysis Set

Race	Study 301 (N=30,346)	US Population
White	79.2%	75.0%
Black or African American	10.2%	14.2%
Asian	4.6%	6.8%
More than one race	2.1%	3.4%
American Indian or Alaska Native	0.8%	1.7%
Hawaiian or other Pacific Islander	0.2%	0.4%
Other	2.0%	5.5%
Not reported or unknown	0.9%	0%
Ethnicity		
Hispanic or Latino	20.5%	18.4%

No difference in race/ethnicity of vaccine vs placebo recipients

EDC, US Census Bureau: ACS Demographic Estimate

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Solicited Adverse Reactions

Study 301 - Solicited Adverse Reaction Safety Set (N=30,338)

Follow-up Period for Safety Data Collection

Vaccine or Placebo

Active Surveillance

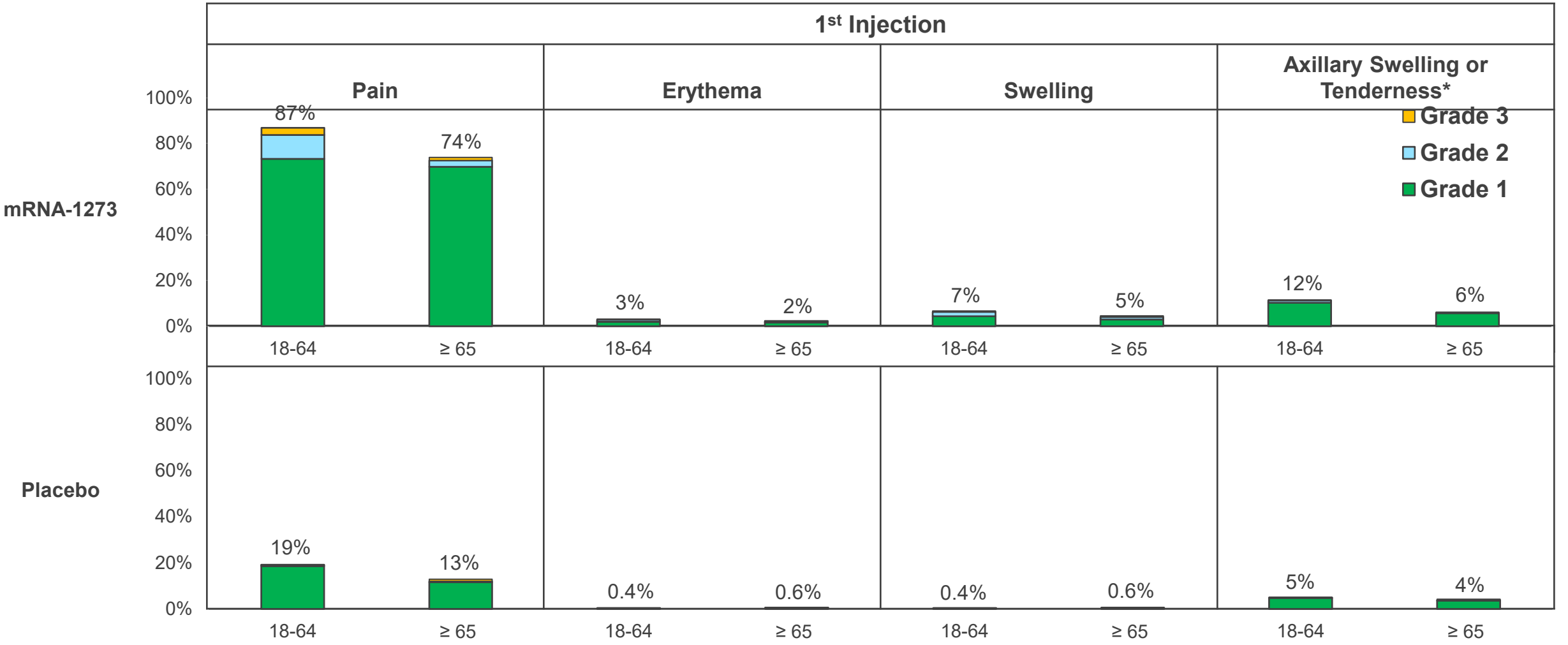
Solicited Adverse Reactions — 7 Days

Unsolicited AEs — 28 Days

SAEs, MAAEs, Deaths, and AEs Leading to Discontinuations → End of Study

Study 301: Most Solicited Local Adverse Reactions Were Mild-to-Moderate (1st Injection)

Solicited Safety Set



Includes reports within 7 days of injection.
***Localized axillary swelling or tenderness ipsilateral to the vaccination arm.**

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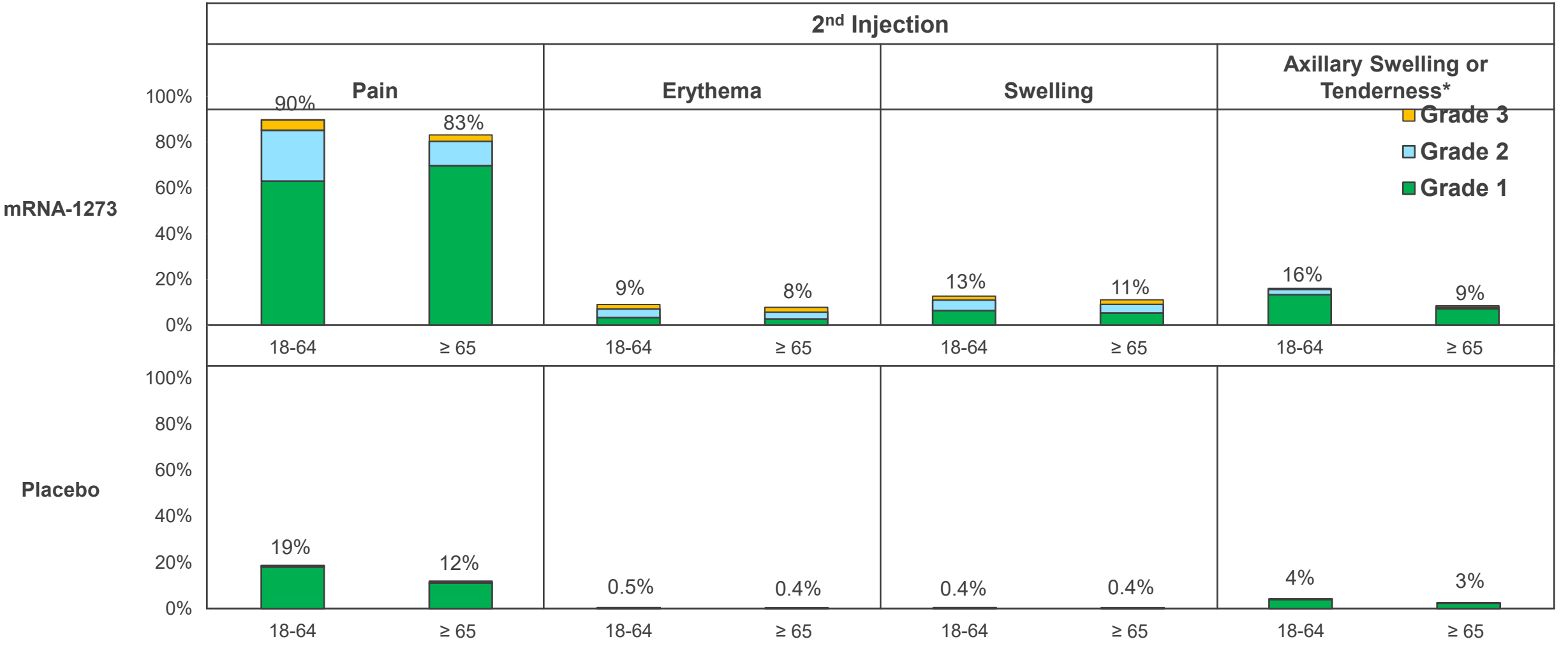
Study 301: Most Solicited Local Adverse Reactions Were Mild-to-Moderate (2nd Injection)

Solicited Safety Set



Includes reports within 7 days of injection.

***Localized axillary swelling or tenderness ipsilateral to the vaccination arm.**

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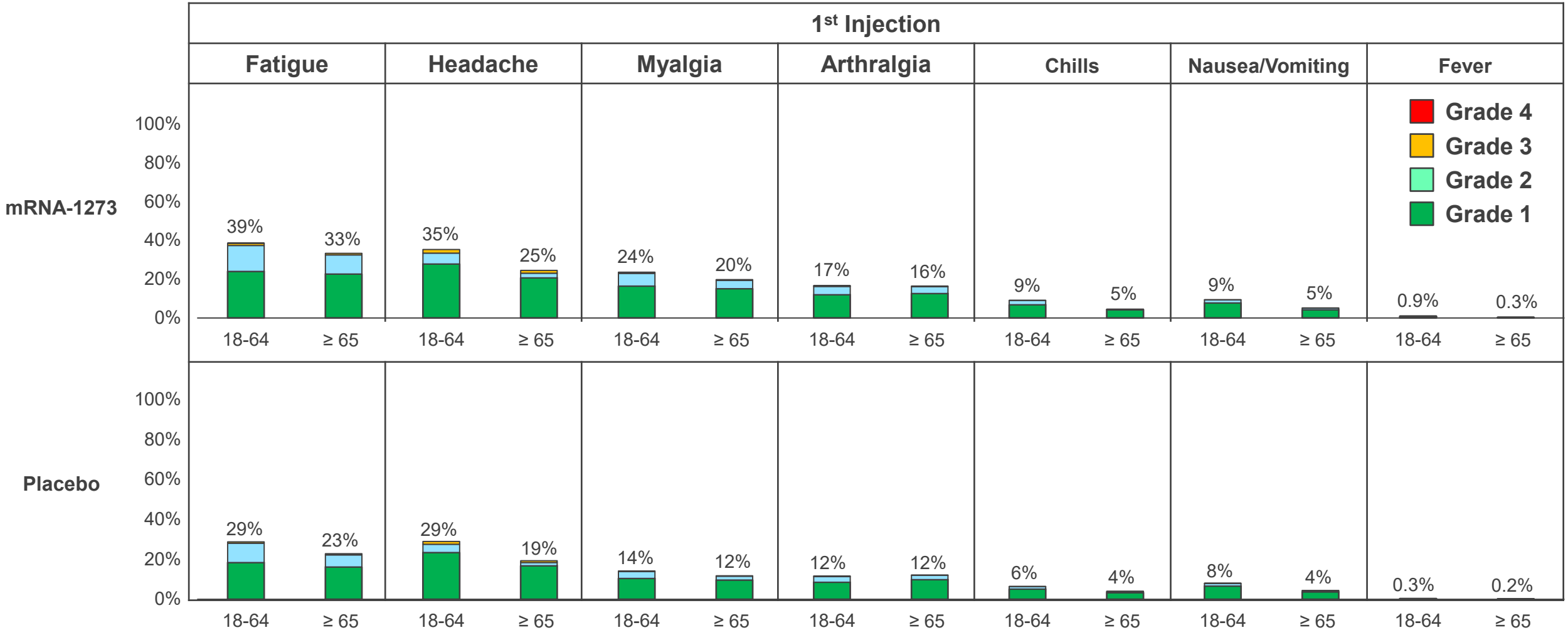
Study 301: Most Solicited Systemic Adverse Reactions Were Mild-to-Moderate (1st Injection)

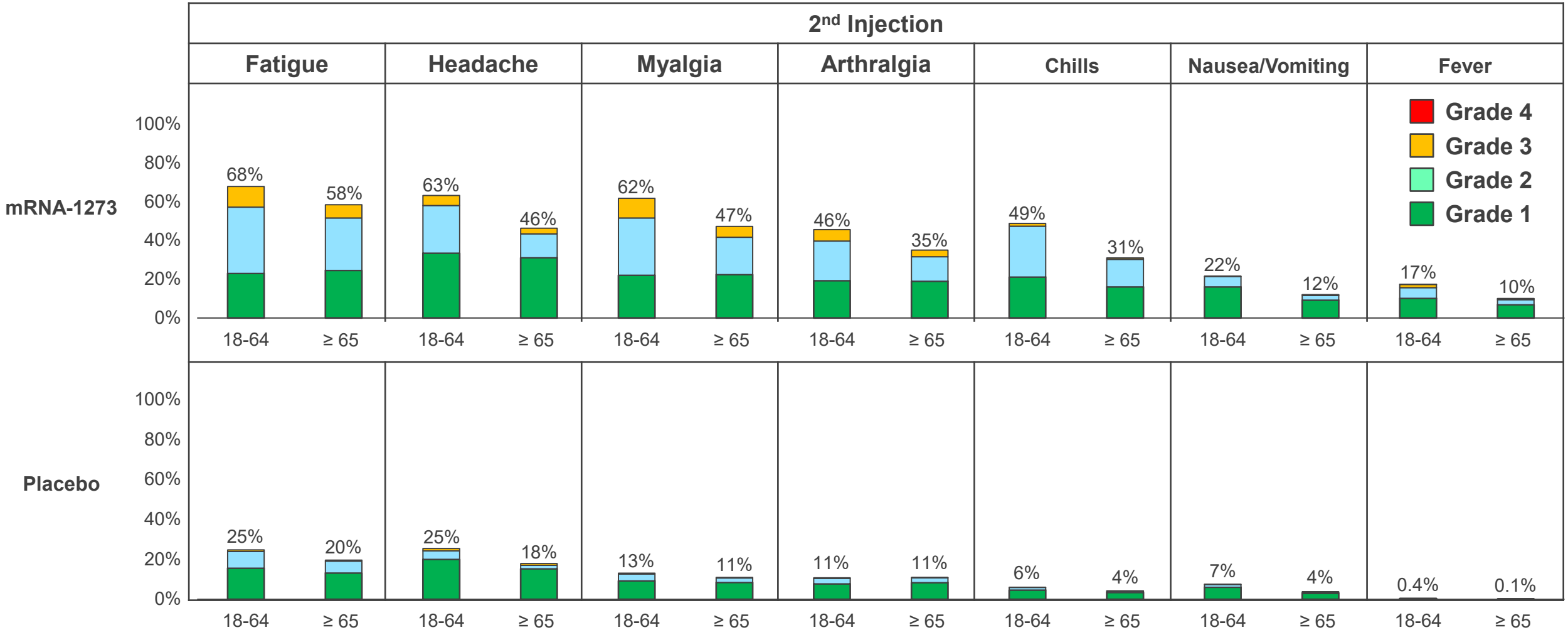
Solicited Safety Set



Solicited Systemic ARs include reports within 7 days of injection

Study 301: Most Solicited Systemic Adverse Reactions Were Mild-to-Moderate (2nd Injection)

Solicited Safety Set



Solicited Systemic ARs include reports within 7 days of injection

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Unsolicited Adverse Events

Study 301 - Safety Set (N=30,346)

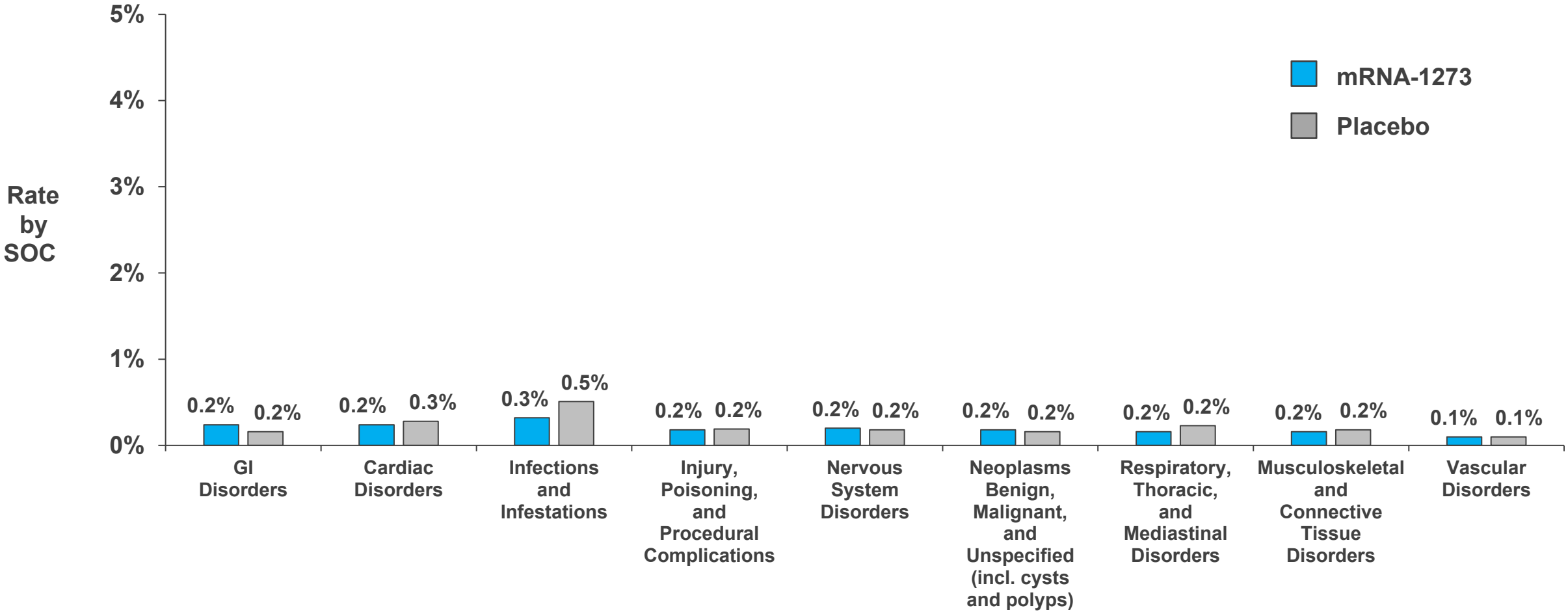
Study 301: Summary of Unsolicited AEs

Safety Set

Unsolicited Adverse Events	mRNA-1273 N = 15,184		Placebo N= 15,162	
	n	%	n	%
Any Adverse Event (within 28 days)	4752	**31.3%**	4338	**28.6%**
Any Medically-Attended Adverse Event (MAAE)	3468	**22.8%**	4131	**27.2%**
Any Serious Adverse Event (SAE)	268	**1.8%**	292	**1.9%**
Any Death (reported through May 4, 2021)	16	**0.1%**	16	**0.1%**

Study 301: Rates of SAEs Were Comparable Between Groups

Safety Set



System Organ Class (SOC) occurring at rate >0.05%
% shown is rounded to nearest 0.1%

Study 301, Part A (Blinded Phase): Myocarditis/Pericarditis
Safety Set

Adverse Event	mRNA-1273 n=15,184	Placebo n=15,162
Myocarditis	0	0
Pericarditis	2	2

Pericarditis in 2 mRNA-1273 vaccine recipients:

- **59-year old female:**
  - **Nonserious chest pain, dyspnea & fatigue Day 4 post dose 2 that resolved within 2 days**
  - **Presented with chest pain & syncope 68 days post dose 2 leading to hospitalization & diagnosis of pericarditis & pericardial effusion, both of which resolved**
  - **Classified as vaccine-related by the investigator**
- **65-year-old male:**
  - **Hospitalized with a diagnosis of pericarditis 73 days post dose 2, resolved the following day**
  - **Occurred 19 days after an SAE of myocardial infarction**
  - **Classified as not vaccine-related by the investigator**

Study 301, Part B (Open Label Phase): Myocarditis/Pericarditis *Safety Set*

Adverse Event	mRNA-1273 n=27,266
Myocarditis	0
Pericarditis	1

Pericarditis in 1 mRNA-1273 vaccine recipient:

- **23-year-old male**
- **Diagnosed with COVID-19 during Part A (Placebo participant) 2 months before receiving 1st dose of mRNA-1273**
- **Bradycardia asymptomatic for a month – no other symptoms**
- **43 days after dose 2 diagnosed with bradycardia and pericardial effusion**
- **Classified as vaccine-related by the investigator**

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Phase 3 COVE Study: Efficacy Through End of Blinded Phase

Background

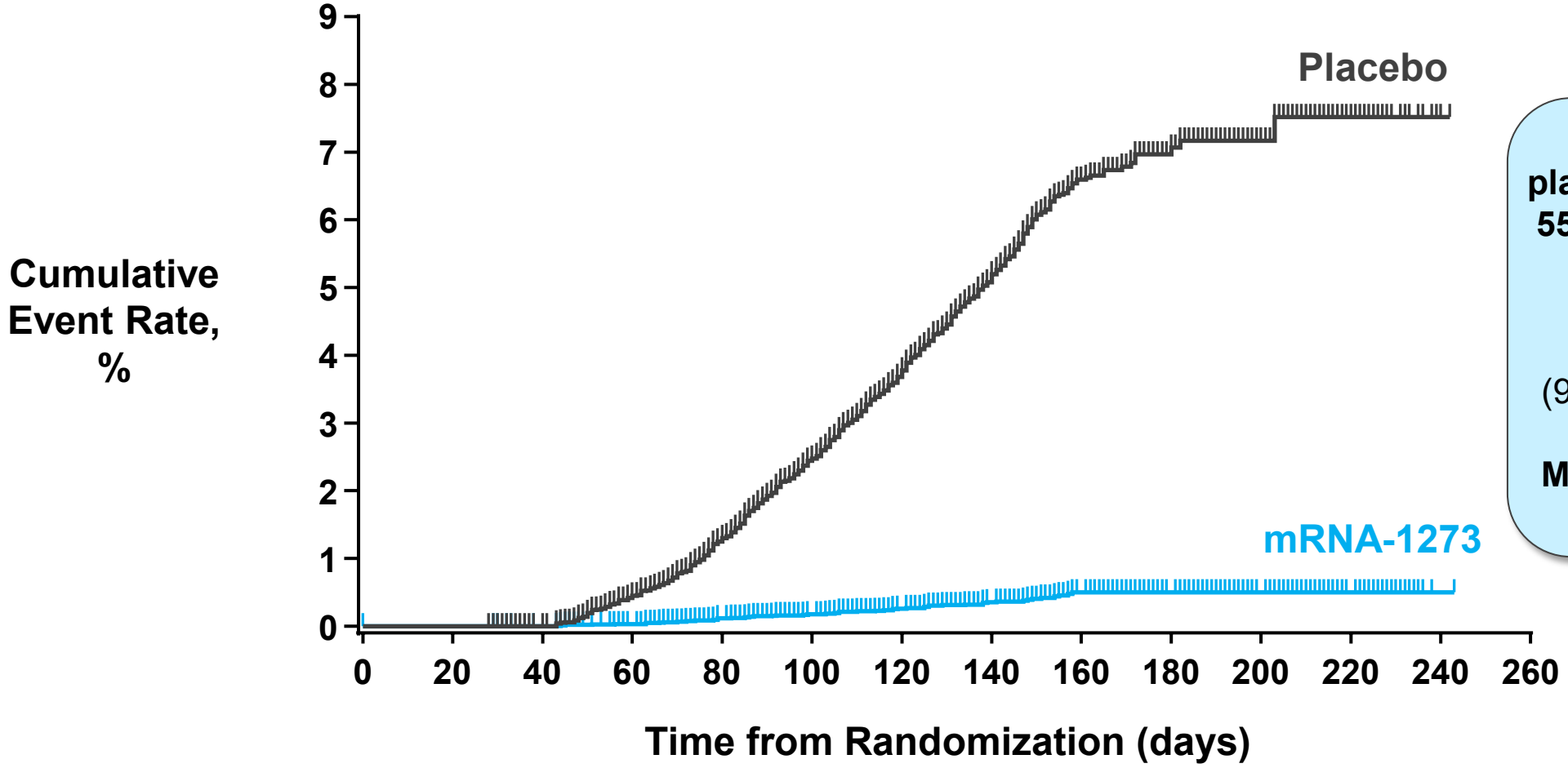
- ~30,000 participants randomized to vaccine or placebo
- Efficacy of mRNA-1273 initially shown to be 94.1% starting 14 days after receipt of a 2-dose regimen in COVE trial[1] (data as of 11/25/20)
  - Results based on median follow-up of 9 weeks post-dose 2
- Efficacy results in BLA updated to a median of 5.3 months follow-up post-dose 2 through end of the blinded phase of the study (data as of 3/26/21)
- After EUA, subjects were offered unblinding and placebo recipients were offered vaccine
- Booster vaccination commenced in Sept, 2021 and is ongoing

[1] Baden et al *NEJM*, 2020

Vaccine Efficacy to Prevent COVID-19 in Individuals ≥18 Years of Age

Cumulative incidence of COVID-19 events starting 14 days after the 2nd dose

Per Protocol Set



744 cases in placebo recipients & 55 cases in vaccine recipients

93.2% Efficacy
(95% CI: 91.0, 94.8)

Median 5.3 months of follow-up

El Sahly, NEJM, 2021

Phase 3 COVE Study: Vaccine Efficacy by Time Increment Post-Dose 2

Incidence rates of COVID-19 based on adjudicated cases by time period

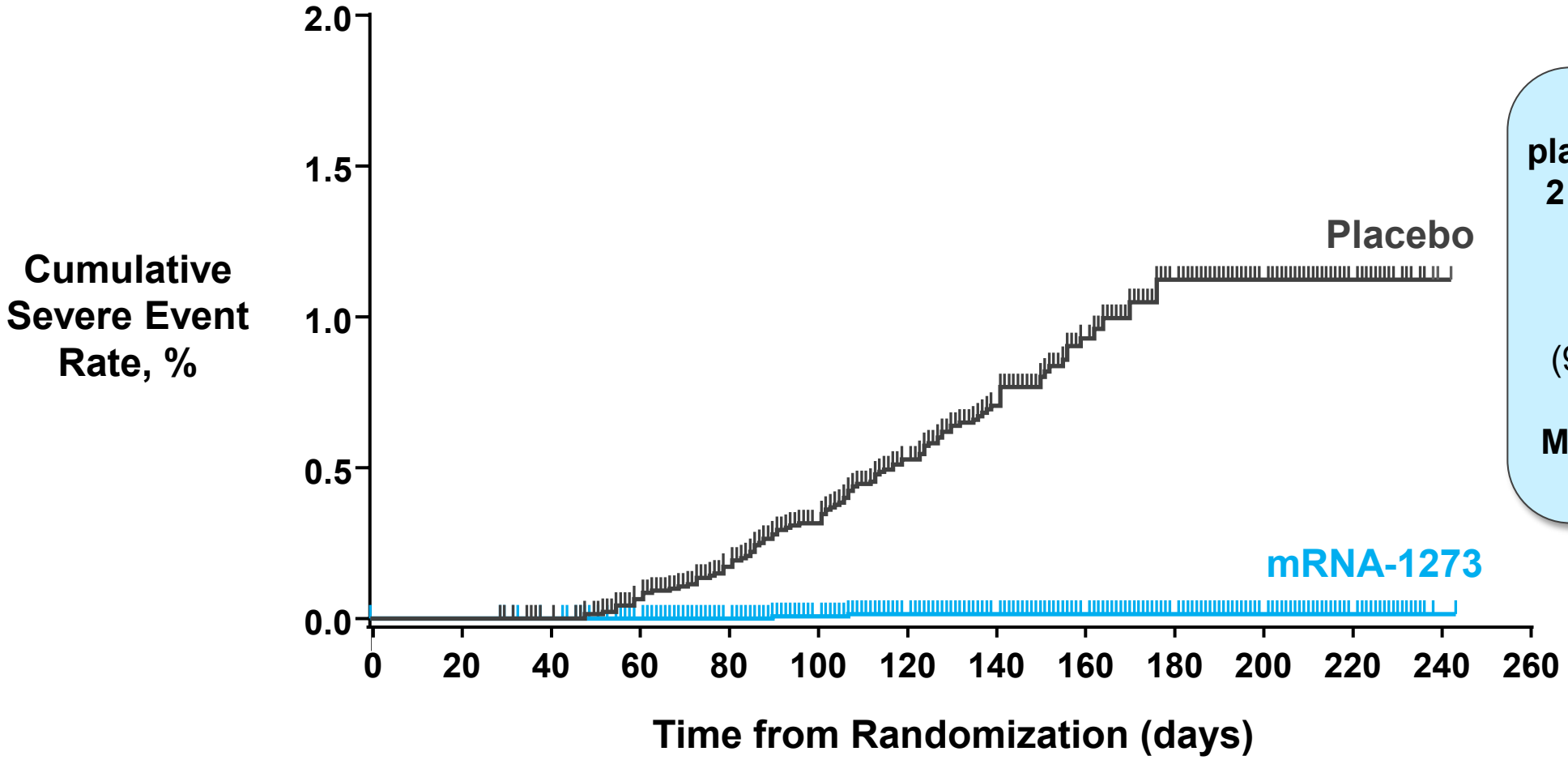
Per-protocol set

First COVID-19 Occurrence[2]	Vaccine Efficacy (%) (95% CI)[3]
≥14 days after dose 2	**93.1%** (90.9, 94.9)
≥14 days after dose 2 to <2 months after dose 2	**91.8%** (86.9, 95.1)
≥ 2 months after dose 2 to <4 months after dose 2	**94.0%** (91.2, 96.1)
≥4 months after dose 2	**92.4%** (84.3, 96.8)

Vaccine Efficacy to Prevent Severe COVID-19 in Individuals ≥18 Years of Age

Cumulative incidence of Severe COVID-19 events starting 14 days after the 2nd dose

Per Protocol Set



106 cases in placebo recipients & 2 cases in vaccine recipients

98.2% Efficacy
(95% CI: 92.8,99.6)

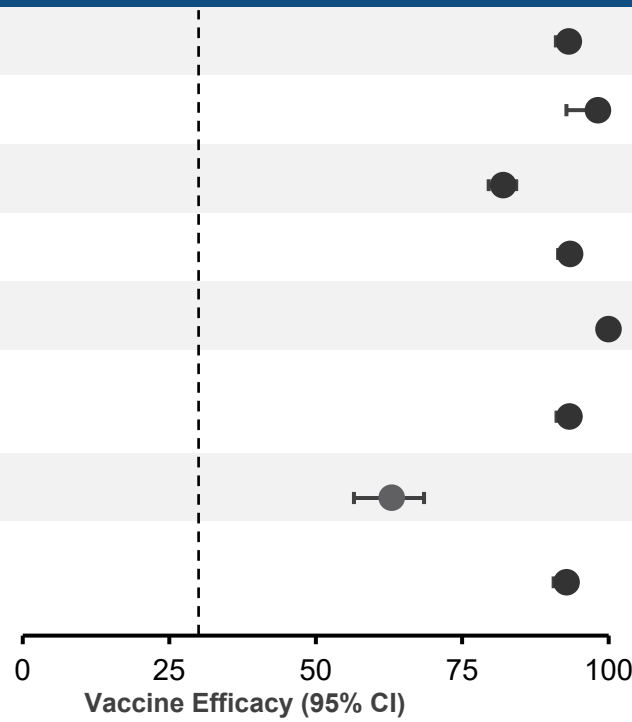
Median 5.3 months of follow-up

El Sahly, NEJM, 2021

Vaccine Efficacy by Primary and Secondary Endpoints – COVE Efficacy Trial (P301)

Per Protocol Set

Subgroup	Number of Events		Vaccine Efficacy (95% CI)
	Placebo N = 14,164	mRNA-1273 N = 14,287	
Covid-19	744	55	93.2% (91.0-94.8)
Severe Covid-19	106	2	98.2% (92.8-99.6)
SARS-CoV-2 Infection	1339	280	82.0% (79.5-84.2)
Covid-19 (Secondary definition - CDC)	807	58	93.4% (91.4-94.9)
Death (Covid-19)	3	0	100% (NE-100.0)
Covid-19 (14 days after first injection)	769	56	93.3% (91.1-94.9)
Asymptomatic	498	214	63.0% (56.6-68.5)
Covid-19 (Regardless of prior SARS-CoV-2)*	754	58	92.8% (90.6-94.5)



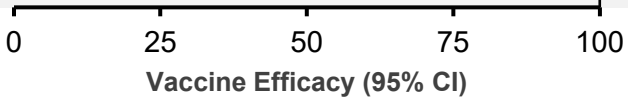
Dotted line represents lower bound of 95% CI for efficacy required for primary endpoint
* Based on Full Analysis Set (N = 15,166 for placebo & 15,180 for mRNA-1273)

Vaccine Efficacy of mRNA-1273 to Prevent COVID-19 by Age, Sex & Race/Ethnicity

COVID-19 events starting 14 days after the 2nd dose

Per-protocol set

Subgroup	# Events/N Placebo N = 14,164	# Events/N mRNA-1273 N = 14,287	Vaccine Efficacy (95% CI)
Overall	744	55	93.2% (91.0-94.8)
Age (Years)			
18 to <65	644/10569	46/10661	93.4% (91.1-95.1)
≥65	100/3595	9/3626	91.5% (83.2-95.7)
65 to <75	81/2898	9/2990	89.7% (79.6-94.9)
≥75	19/697	0/636	100% (NE-100.0)
Sex			
Male	378/7494	30/7439	92.5% (89.1-94.8)
Female	366/6670	25/6848	93.8% (90.7-95.9)
Race*			
White	631/11273	48/11391	93.0% (90.6-94.7)
Black or African American	41/1352	4/1391	91.1% (75.2-96.8)
Asian	29/700	1/628	96.5% (74.2-99.5)
American Indian or Alaska Native	5/113	0/109	100% (NE-100.0)
Native Hawaiian or Other Pacific Islander	0/31	0/36	NE (NE-NE)
Ethnicity†			
Hispanic or Latino	177/2787	10/2831	94.8% (90.2-97.3)
Not Hispanic or Latino	563/11249	45/11322	92.6% (90.0-94.5)



Summary of SPIKEVAX in Individuals ≥18 Years of Age

Safety

- Vaccine well tolerated in individuals ≥18 year olds
  - Pain was the most commonly reported local reaction
  - Fatigue, headache, myalgia, and arthralgia most commonly reported systemic reactions
  - Systemic reactions more common after dose 2 than dose 1
  - No difference in adverse reactions for 18-64 years vs ≥65 years

Efficacy

- After median 5.3 months follow-up:
  - 93.2% efficacy against COVID-19 starting 14 days after dose 2 (per protocol)
  - 98.2% efficacy against severe COVID-19 starting 14 days after dose 2 (per protocol)
  - 82.0% reduction of SARS-CoV-2 infection regardless of symptoms starting 14 days after dose 2 (per protocol)
  - 63.0% reduction in asymptomatic SARS-CoV-2 infection starting 14 days after dose 2 (per protocol)
  - Efficacy consistent regardless of risk factors, age, gender, or race/ethnicity

THANK YOU!

- NIH/COV-PN
- All investigators at many study sites
- Study site personnel
- BARDA
- NIAID
- Laboratory at Duke University

Most importantly, the many individuals who participated in these trials

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