Phase II, open-label study to assess the safety and immunogenicity of Fluzone® High-Dose Quadrivalent (Influenza Vaccine), 2021–2022 Formulation and a third dose of mRNA-1273 COVID-19 vaccine (Moderna) administered either concomitantly or singly in adults 65 years of age and older previously vaccinated with a 2-dose schedule of mRNA-1273 vaccine

Study Code: QHD00028

https://clinicaltrials.gov/ct2/show/NCT04969276

In partnership with:

- The Biomedical Advanced Research and Development Authority, part of the office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services
- Moderna, Inc.

SANOFI PASTEUR

Ruvim Izikson, MD, MPH

October 20th, 2021

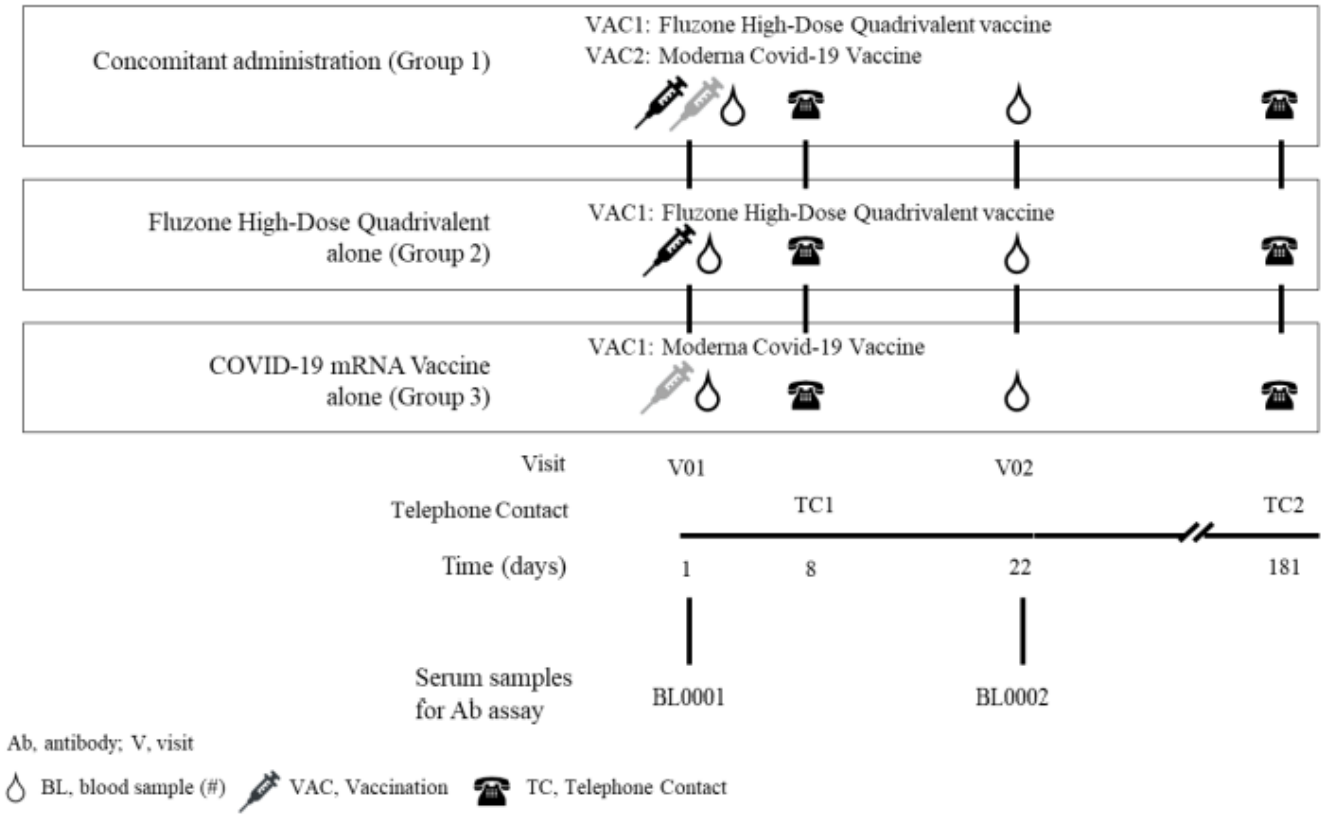
Rationale for vaccine selection and study group

- **Adults 65 years of age and older are a critical priority for influenza and COVID-19 immunizations due to the risk of severe complications**
- **Based on the COVID-19 vaccine primary series timing and strategy, older adults are most likely eligible for COVID-19 boosters and their annual influenza vaccine during the same window of time**
  - This creates the risk that many get vaccinated only for one or the other; with priority on COVID-19, influenza is more likely the missed vaccine
- **QIV-HD is the most frequently administered influenza vaccine to individuals 65 years of age and older in the US[1]**
- **100µg mRNA-1273 vaccine dose was selected based on projected regulatory expectations at the time of study start**

1. Internal calculations by Sanofi based on IQVIA database of total flu vaccines administered from 8/20-3/21 in adults 65+. Study details and information maintained by Sanofi

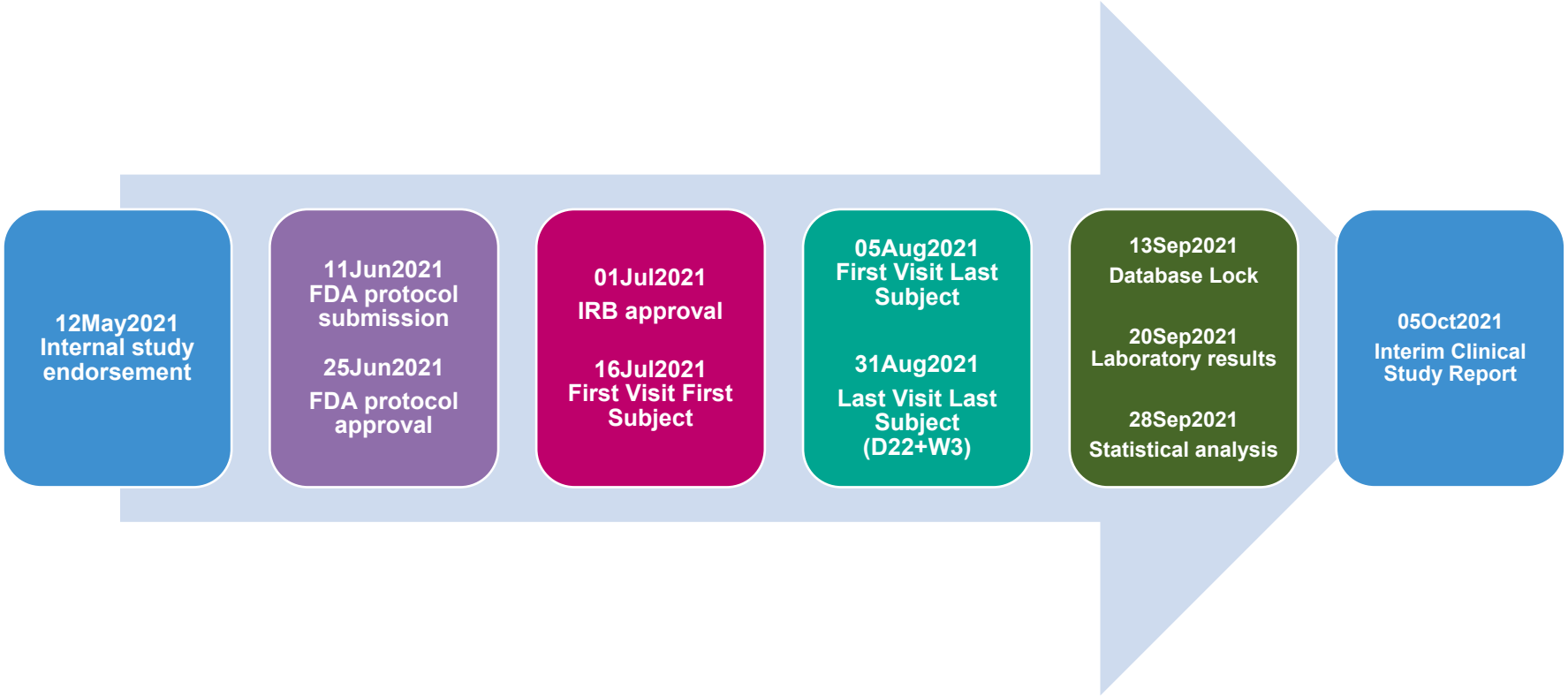
Study Design

- **Descriptive study with ~300 participants (100 per group)**
- **Randomized, open label, conducted in the US**
- **Participants received 2 doses of mRNA-1273 vaccine at least 5 months before enrollment**
- **mRNA-1273 vaccine booster dose (100µg)**
- **QIV-HD 2021-2022 formulation (240µg)**
  - Offered to Group 3 participants at D22 as part of routine medical care



SANOFI PASTEUR

Study Timeline



Demographics by treatment group

	Group 1 QIV-HD+mRNA-1273 (N=100) n (%)	Group 2 QIV-HD (N=92) n (%)	Group 3 mRNA-1273 (N=104) n (%)	All (N=296) n (%)
Sex: n (%)				
Male	46 (46.0)	43 (46.7)	41 (39.4)	130 (43.9)
Female	54 (54.0)	49 (53.3)	63 (60.6)	166 (56.1)
Missing	0	0	0	0
Sex ratio: Male/Female	0.85	0.88	0.65	0.78
Age (year)				
M	100	92	104	296
Mean (SD)	71.3 (4.74)	71.8 (5.20)	72.0 (4.91)	71.7 (4.94)
Min ; Max	65.0; 85.0	65.0; 89.0	65.0; 86.0	65.0; 89.0
Median	71.0	71.0	72.0	71.0
Q1 ; Q3	67.5; 74.0	68.0; 74.5	69.0; 74.0	68.0; 74.0
Age subgroup: n(%)				
65-<75 years	77 (77.0)	69 (75.0)	79 (76.0)	225 (76.0)
>=75 years	23 (23.0)	23 (25.0)	25 (24.0)	71 (24.0)
>=75-<85	22 (22.0)	20 (21.7)	23 (22.1)	65 (22.0)
>=85 years	1 (1.0)	3 (3.3)	2 (1.9)	6 (2.0)

n: number of participants fulfilling the item listed
M: number of participants with available data for the relevant endpoint
Q1; Q3: first quartile; third quartile
The age of a participant in the study was the calendar age in years only.

Demographics by treatment group

	Group 1 QIV-HD+mRNA-1273 (N=100) n (%)	Group 2 QIV-HD (N=92) n (%)	Group 3 mRNA-1273 (N=104) n (%)	All (N=296) n (%)
Ethnicity: n (%)				
Hispanic or Latino	4 (4.0)	2 (2.2)	2 (1.9)	8 (2.7)
Not Hispanic or Latino	93 (93.0)	89 (96.7)	100 (96.2)	282 (95.3)
Not reported	1 (1.0)	1 (1.1)	1 (1.0)	3 (1.0)
Unknown	2 (2.0)	0	1 (1.0)	3 (1.0)
Racial origin: n (%)				
American Indian or Alaska Native	0	0	0	0
Asian	2 (2.0)	0	0	2 (0.7)
Black or African American	1 (1.0)	4 (4.3)	0	5 (1.7)
Native Hawaiian or other Pacific Islander	0	1 (1.1)	2 (1.9)	3 (1.0)
White	94 (94.0)	86 (93.5)	102 (98.1)	282 (95.3)
Multiple	1 (1.0)	1 (1.1)	0	2 (0.7)
Unknown	0	0	0	0
Not reported	2 (2.0)	0	0	2 (0.7)

n: number of participants fulfilling the item listed
M: number of participants with available data for the relevant endpoint

Study objectives

Safety

- To describe the safety profile of QIV-HD and mRNA-1273 vaccine administered concomitantly or singly
  - Solicited injection site reactions and systemic reactions occurring through 7 days after injection
  - Unsolicited systemic adverse events through 21 days after vaccination
  - Serious adverse events (SAEs), adverse events of special interest (AESIs) and medically-attended adverse events (MAAEs) through 6 months after vaccination

Immunogenicity

- To describe the immune response elicited by QIV-HD administered concomitantly or singly, in each study intervention group
- To describe the immune response elicited by mRNA-1273 vaccine administered concomitantly or singly, in each study intervention group

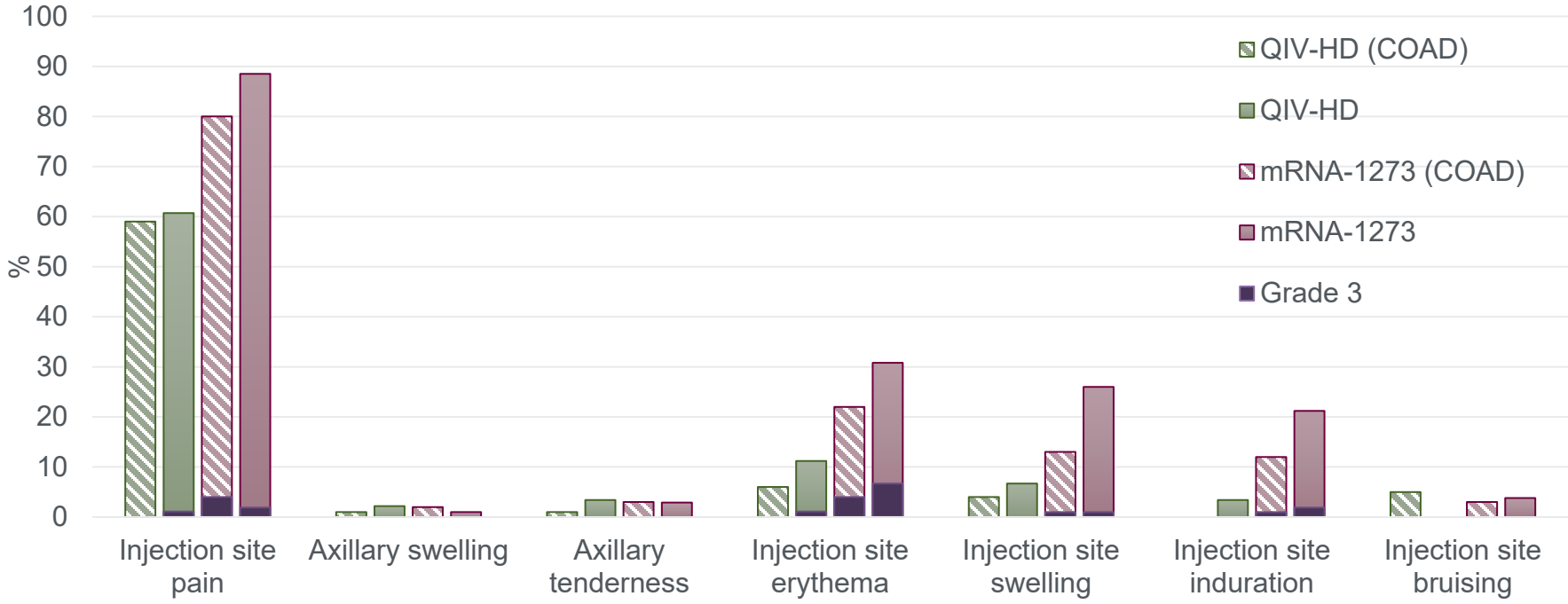
Summary of solicited reactions (Day 1 - 8)

Participants experiencing at least one:	Group 1 QIV-HD + mRNA-1273 (N=100) n/M	%	(95% CI)	Group 2 QIV-HD (N=92) n/M	%	(95% CI)	Group 3 mRNA-1273 (N=104) n/M	%	(95% CI)
Solicited reaction	94/100	94.0	(87.4; 97.8)	65/89	73.0	(62.6; 81.9)	100/104	96.2	(90.4; 98.9)
Grade 3 solicited reaction	17/100	17.0	(10.2; 25.8)	3/89	3.4	(0.7; 9.5)	19/104	18.3	(11.4; 27.1)
Solicited injection site reaction	86/100	86.0	(77.6; 92.1)	55/89	61.8	(50.9; 71.9)	95/104	91.3	(84.2; 96.0)
After injection of QIV-HD	61/100	61.0	(50.7; 70.6)	55/89	61.8	(50.9; 71.9)	-	-	-
After injection of mRNA-1273	82/100	82.0	(73.1; 89.0)	-	-	-	95/104	91.3	(84.2; 96.0)
Grade 3 injection site reaction	8/100	8.0	(3.5; 15.2)	2/89	2.2	(0.3; 7.9)	8/104	7.7	(3.4; 14.6)
After injection of QIV-HD	0/100	0	(0; 3.6)	2/89	2.2	(0.3; 7.9)	-	-	-
After injection of mRNA-1273	8/100	8.0	(3.5; 15.2)	-	-	-	8/104	7.7	(3.4; 14.6)
Solicited systemic reaction	80/100	80.0	(70.8; 87.3)	44/89	49.4	(38.7; 60.2)	87/104	83.7	(75.1; 90.2)
Grade 3 systemic reaction	13/100	13.0	(7.1; 21.2)	1/89	1.1	(0; 6.1)	14/104	13.5	(7.6; 21.6)

n: number of participants experiencing the endpoint listed in the first column
M: number of participants with available data for the relevant endpoint

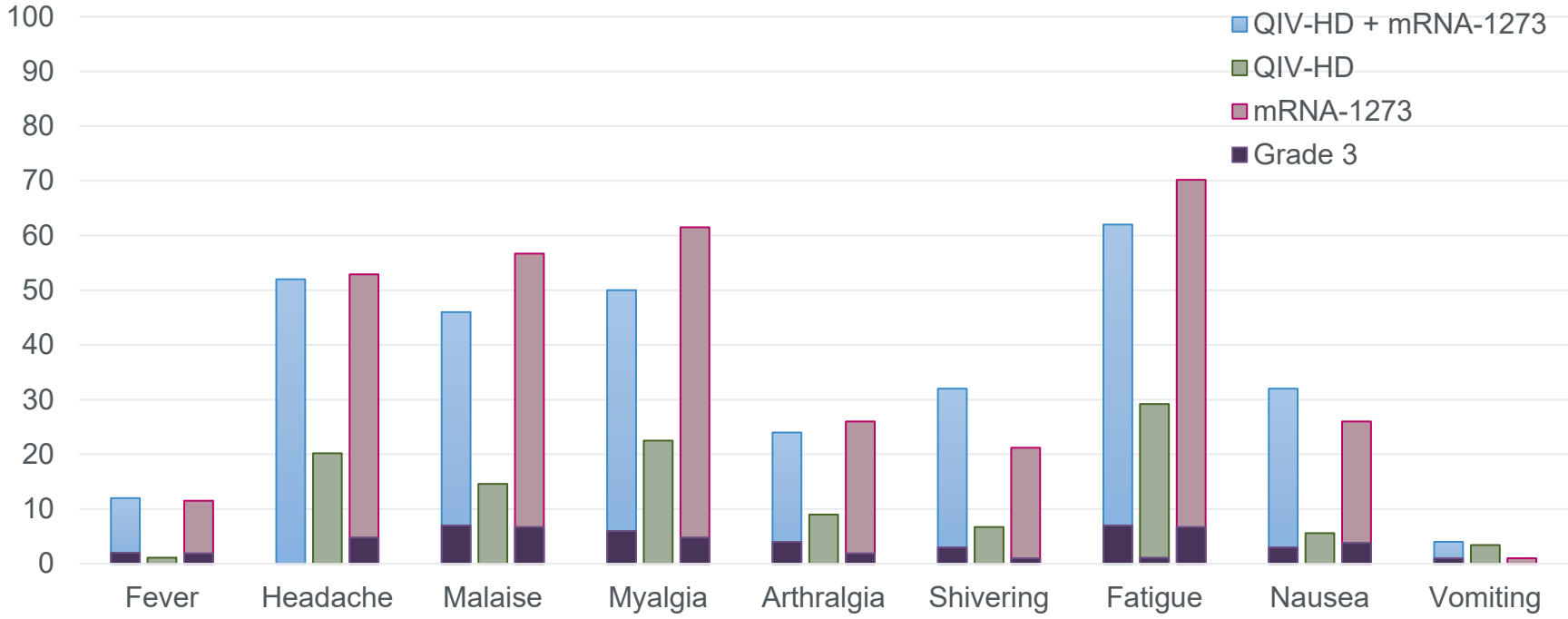
Grade 3: A type of adverse event that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention.
Grade 3: > 100 mm

Solicited injection site reactions (Day 1 - 8)



Grade 3: A type of adverse event that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention.
Grade 3: > 100 mm

Solicited systemic reactions (Day 1 - 8)



Grade 3: A type of adverse event that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention.

Grade 3: ≥ 39.0°C **or** ≥ 102.1°F

Unsolicited adverse events through 21 days

	Group 1 QIV-HD + mRNA-1273 (N=100)				Group 2 QIV-HD (N=92)				Group 3 mRNA-1273 (N=104)			
Participants experiencing at least one:	**n**	**%**	**(95% CI)**	**nAEs**	**n**	**%**	**(95% CI)**	**nAEs**	**n**	**%**	**(95% CI)**	**nAEs**
Immediate unsolicited AE	1	1.0	(0; 5.4)	3	1	1.1	(0; 5.9)	1	0	0	(0; 3.5)	0
Grade 3 immediate unsolicited AE	1	1.0	(0; 5.4)	1	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0
Immediate unsolicited AR	0	0	(0; 3.6)	0	1	1.1	(0; 5.9)	1	0	0	(0; 3.5)	0
Grade 3 immediate unsolicited AR	0	0	(0; 3.6)	0	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0
Unsolicited AE	17	17.0	(10.2; 25.8)	23	10	10.9	(5.3; 19.1)	12	15	14.4	(8.3; 22.7)	24
Grade 3 unsolicited AE	1	1.0	(0; 5.4)	1	1	1.1	(0; 5.9)	1	0	0	(0; 3.5)	0
Unsolicited AR	6	6.0	(2.2; 12.6)	7	4	4.3	(1.2; 10.8)	5	7	6.7	(2.7; 13.4)	10
Grade 3 unsolicited AR	0	0	(0; 3.6)	0	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0
Unsolicited injection site AR	2	2.0	(0.2; 7.0)	3	1	1.1	(0; 5.9)	1	1	1.0	(0; 5.2)	1
After injection of QIV-HD	1	1.0	(0; 5.4)	1	1	1.1	(0; 5.9)	1	0	0	(0; 3.5)	0
After injection of mRNA COVID-19	2	2.0	(0.2; 7.0)	2	0	0	(0; 3.9)	0	1	1.0	(0; 5.2)	1
Grade 3 unsolicited injection site AR	0	0	(0; 3.6)	0	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0
After injection of QIV-HD	0	0	(0; 3.6)	0	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0
After injection of mRNA COVID-19	0	0	(0; 3.6)	0	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0
Unsolicited systemic AE	15	15.0	(8.6; 23.5)	20	9	9.8	(4.6; 17.8)	11	14	13.5	(7.6; 21.6)	23
Grade 3 unsolicited systemic AE	1	1.0	(0; 5.4)	1	1	1.1	(0; 5.9)	1	0	0	(0; 3.5)	0
Unsolicited systemic AR	4	4.0	(1.1; 9.9)	4	3	3.3	(0.7; 9.2)	4	6	5.8	(2.1; 12.1)	9
Grade 3 Unsolicited systemic AR	0	0	(0; 3.6)	0	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0
SAE	0	0	(0; 3.6)	0	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0
Grade 3 SAE	0	0	(0; 3.6)	0	0	0	(0; 3.9)	0	0	0	(0; 3.5)	0

n: number of participants experiencing the endpoint listed in the first column; n AEs: number of AEs

Medically-attended adverse events through day 22

Participants experiencing at least one:	All MAAEs n	%	(95% CI)	n MAAEs	Related MAAEs n	%	(95% CI)	n MAAEs
Group 1 / QIV-HD + mRNA-1273 (N=100)								
MAAEs	3	3.0	(0.6; 8.5)	3	0	0	(0; 3.6)	0
Infections and infestations	1	1.0	(0; 5.4)	1	0	0	(0; 3.6)	0
Localized infection	1	1.0	(0; 5.4)	1	0	0	(0; 3.6)	0
Injury, poisoning and procedural complications	2	2.0	(0.2; 7.0)	2	0	0	(0; 3.6)	0
Limb injury	1	1.0	(0; 5.4)	1	0	0	(0; 3.6)	0
Patella fracture	1	1.0	(0; 5.4)	1	0	0	(0; 3.6)	0
Group 2 / QIV-HD (N=92)								
MAAEs	1	1.1	(0; 5.9)	1	0	0	(0; 3.9)	0
Injury, poisoning and procedural complications	1	1.1	(0; 5.9)	1	0	0	(0; 3.9)	0
Skin abrasion	1	1.1	(0; 5.9)	1	0	0	(0; 3.9)	0
Group 3 / mRNA-1273 (N=104)								
MAAEs	3	2.9	(0.6; 8.2)	3	1	1.0	(0; 5.2)	1
Injury, poisoning and procedural complications	1	1.0	(0; 5.2)	1	0	0	(0; 3.5)	0
Spinal compression fracture	1	1.0	(0; 5.2)	1	0	0	(0; 3.5)	0
Musculoskeletal and connective tissue disorders	1	1.0	(0; 5.2)	1	1	1.0	(0; 5.2)	1
Muscle spasms	1	1.0	(0; 5.2)	1	1	1.0	(0; 5.2)	1
Nervous system disorders	1	1.0	(0; 5.2)	1	0	0	(0; 3.5)	0
Radiculopathy	1	1.0	(0; 5.2)	1	0	0	(0; 3.5)	0

n: number of participants experiencing the endpoint listed in the first column; n MAAEs: number of MAAEs
Related: relationship reported by Investigator as related. If the relationship is missing, the MAAEs will be considered as related.

Medically Attended AE (MAAE):
A new onset or a worsening of a condition that prompts to seek unplanned medical advice at a physician's office or Emergency Department

Safety summary (Solicited Reactions)

- **Injection site reactions**
  - QIV-HD: injection site reaction frequency was similar whether the vaccine was administered concomitantly or singly.
  - mRNA-1273: injection site reaction frequency was similar whether vaccine was administered concomitantly or singly.
    - Injection site pain was the most frequently reported injection site reaction for both vaccines. The frequency of injection site pain tended to be lower following injection of QIV-HD.
    - The frequency of Grade 3 injection site reactions tended to be lower following injection of QIV-HD compared to mRNA-1273.
- **Systemic reactions**
  - Fatigue was most frequently reported in all treatment groups. The frequency was similar in the co-administration group and mRNA-1273 group and lower in QIV-HD group.
  - Frequency of Grade 3 systemic reactions was similar in the co-administration group and mRNA-1273 group and lower in QIV-HD group.

Safety summary

- No SAEs, AESIs or deaths.
- No AEs leading to study discontinuation.

MAAEs

- One participant in the mRNA-1273 (alone) group experienced a MAAE assessed as related (PT: muscle spasms).

Unsolicited AEs and ARs

- The frequency of unsolicited AEs and ARs was similar across treatment groups
  - Most unsolicited AEs were systemic in nature.
  - In co-administration group and QIV-HD group, one participant in each reported a Grade 3 unsolicited AE.
  - One participant in the QIV-HD (alone) group with an immediate unsolicited AR (PT: dizziness).

Study Objectives

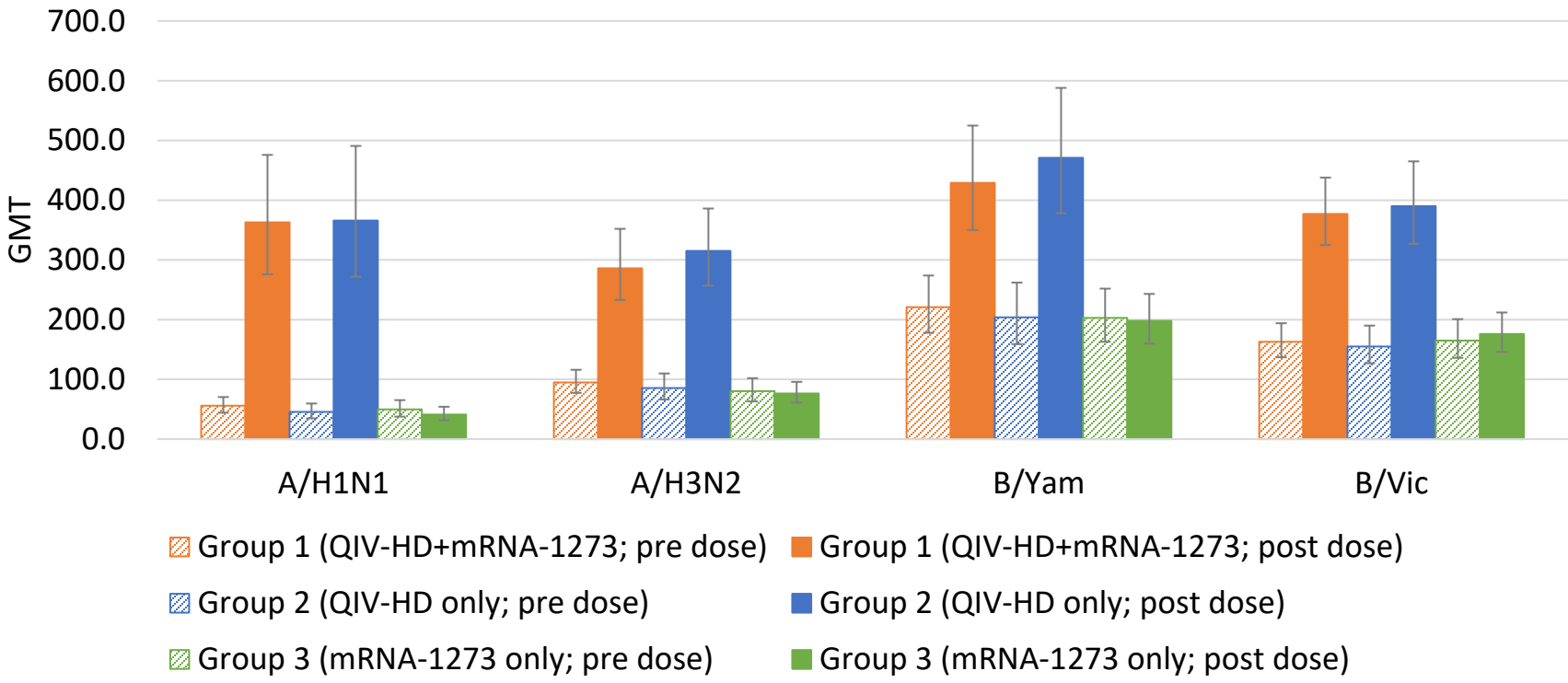
Safety

- To describe the safety profile of QIV-HD and mRNA-1273 vaccine administered concomitantly or singly
  - Solicited injection site reactions and systemic reactions occurring through 7 days after injection
  - Unsolicited systemic adverse events through 21 days after vaccination
  - Serious adverse events (SAEs), adverse events of special interest (AESIs) and medically-attended adverse events (MAAEs) through 6 months after vaccination

Immunogenicity

- To describe the immune response elicited by QIV-HD administered concomitantly or singly, in each study intervention group
- To describe the immune response elicited by mRNA-1273 vaccine administered concomitantly or singly, in each study intervention group

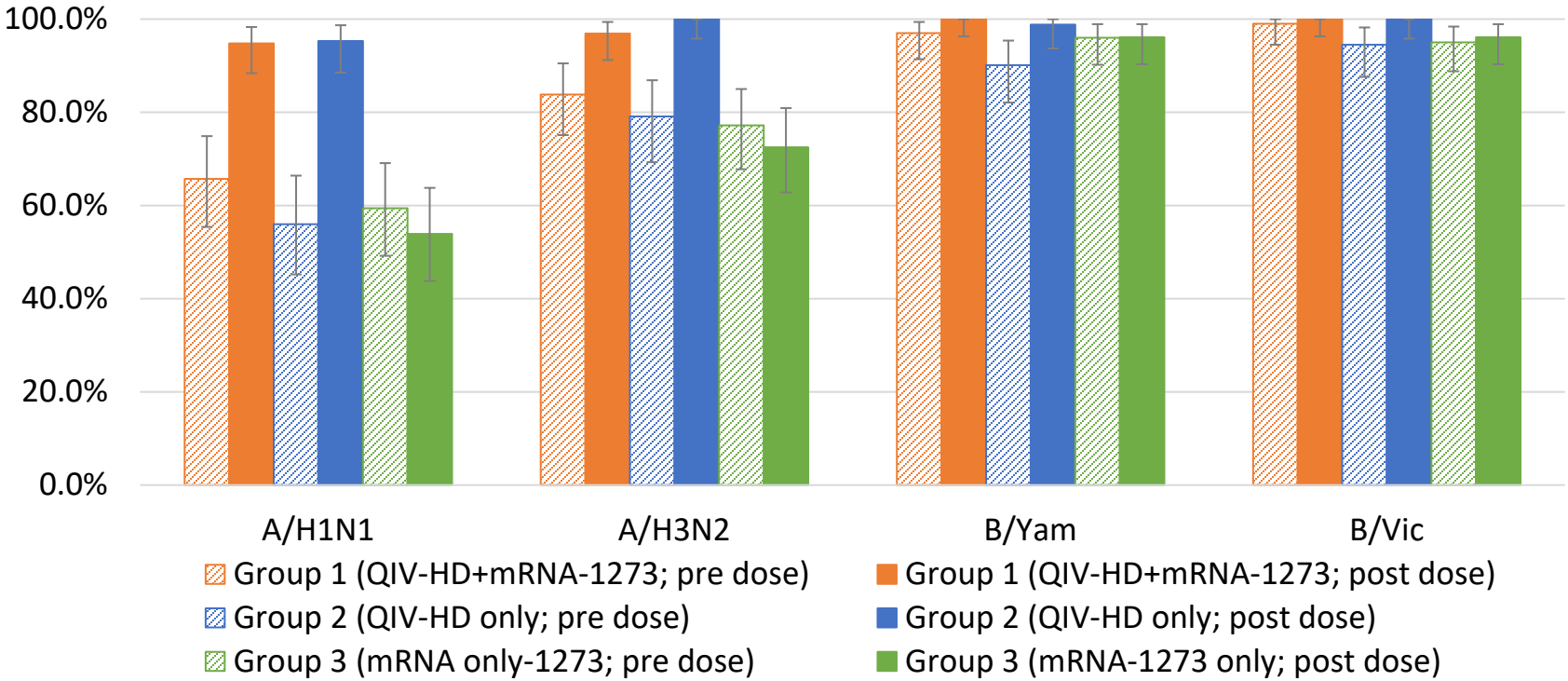
Geometric mean titer of influenza HA antibody response (pre- and post- vaccination), by strain and group



SANOFI PASTEUR

Abbreviation: GMT=geometric mean titer

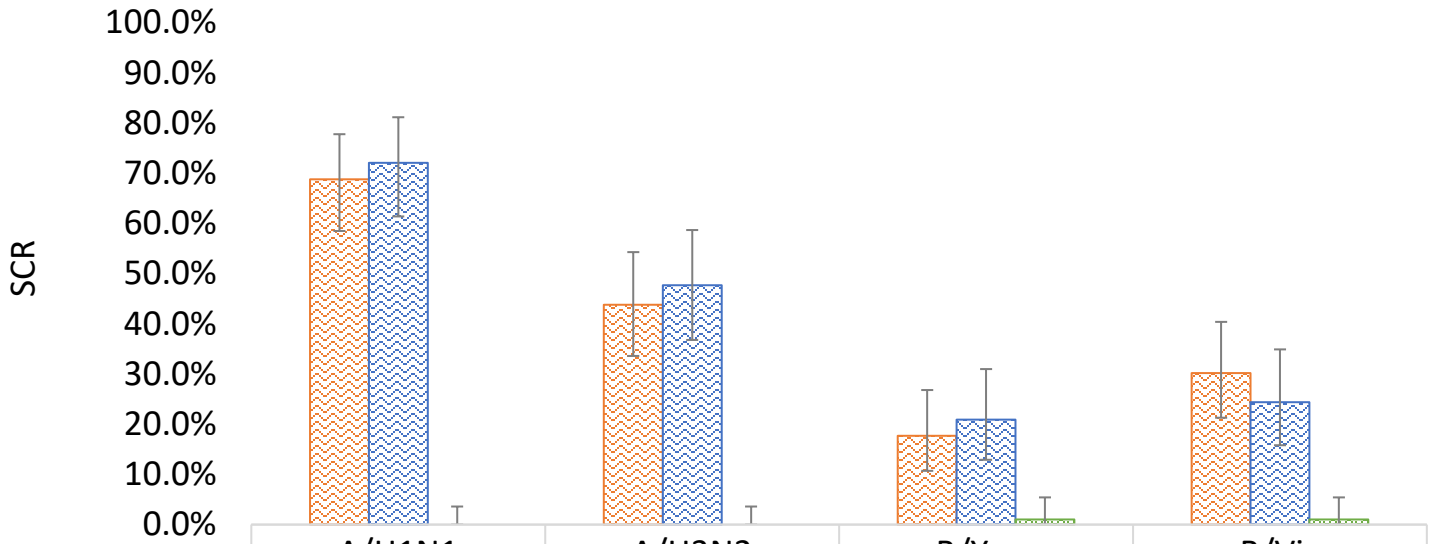
Influenza HA antibody titer ≥1:40 (pre and post vaccination), by strain and group



SANOFI PASTEUR

HAI titer ≥ 40 (1/dil) on D01 and 21 days after injection of QIV-HD (D22)

Seroconversion rate of influenza HA antibody response, by strain and by group



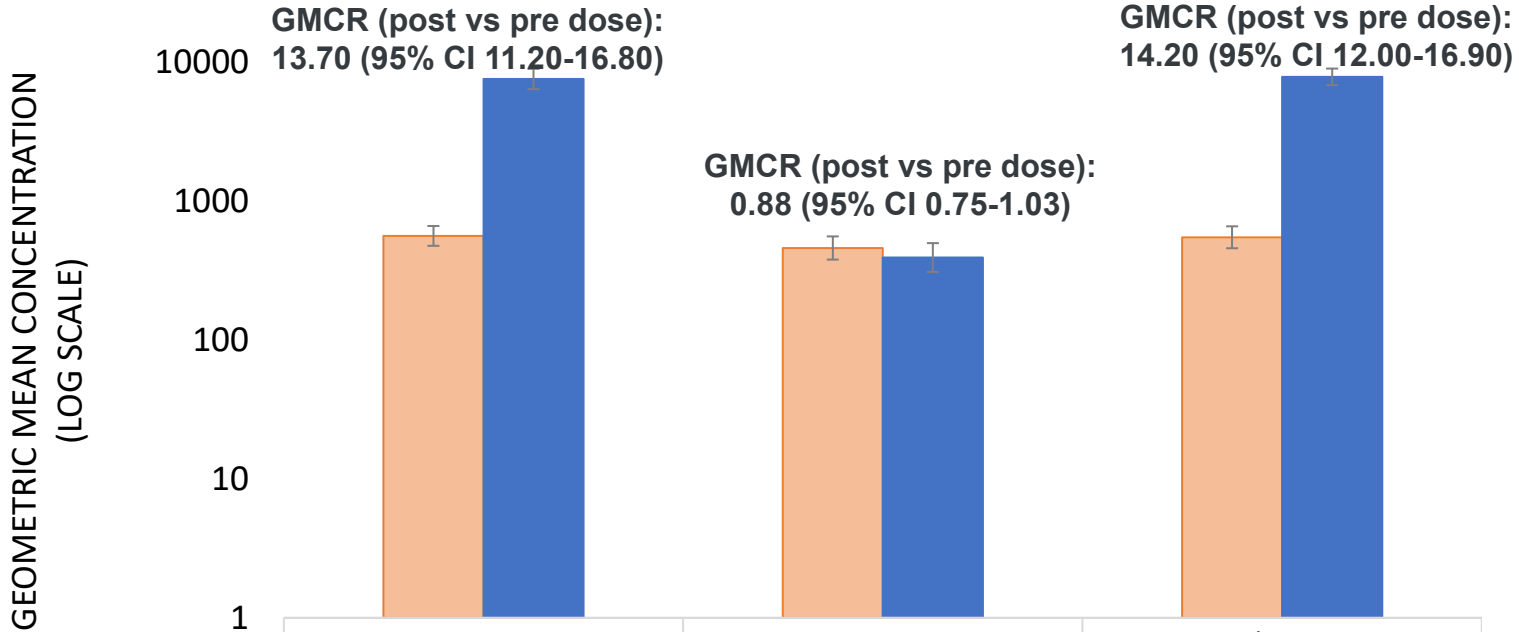
	A/H1N1	A/H3N2	B/Yam	B/Vic
Group 1 (QIV-HD+mRNA-1273)	68.8%	43.8%	17.7%	30.2%
Group 2 (QIV-HD only)	72.1%	47.7%	20.9%	24.4%
Group 3 (mRNA-1273 only)	0.0%	0.0%	1.0%	1.0%

SANOFI PASTEUR

Abbreviation: SCR=seroconversion rate

Definition: titer < 10 [1/dil] at D01 and post-vaccination titer ≥ 40 [1/dil] at D22, or titer ≥ 10 [1/dil] at D01 and a ≥ 4-fold-rise in titer [1/dil] at D22

Antibody response to SARS-CoV-2 by ELISA



	Group 1 (QIV-HD+mRNA-1273)	Group 2 (QIV-HD only)	Group 3 (mRNA-1273 only)
Pre dose GMC (primary axis)	**565 (479; 666)**	**462 (382; 560)**	**552 (461; 662)**
Post dose GMC (primary axis)	**7634 (6445; 9042)**	**395 (311; 502)**	**7904 (6883; 9077)**

SANOFI PASTEUR

Abbreviation: GMC=geometric mean concentration; GMCR=geometric mean concentration ratio

Immunogenicity summary

HAI immune response

- All 3 treatment groups demonstrated similar GMT levels at baseline
- At day 22, the co-administration group and QIV-HD group demonstrated similar GMT levels, proportions of participants with titers ≥ 1:40, and seroconversion rates for each influenza strain.

SARS-CoV-2 immune response

- All 3 treatment groups demonstrated similar GMC levels at baseline.
- At day 22, the co-administration group and mRNA-1273 group demonstrated similar GMC levels and proportions of participants with ≥ 2- and ≥ 4-fold-rise of antibody titers.

Overall interpretation

The QHD00028 study results demonstrate that QIV-HD and mRNA-1273 vaccine (100µg) can be administered safely together without evidence of immunogenicity interference, supporting existing co-administration recommendations of COVID-19 and influenza vaccines.

Much thanks for the collaboration and support from:

Sanofi Pasteur

- **US:** L. Perez, A. Collins, T. Washington, D. Ecker, M. Stirr, D. Divito, B. D'Arienzo, J. Olsommer, J. Soreth-Harman, N. Lupinsky, H. Kabler, M. Martin, C. Rizzo, M. Greenberg
- **Global:** S. Samson, M. Fournier, S. Wagué, P. Bourron, C. Salamand, C. Tabar, JS Bolduc, N. Sater, R. Fernando, S. Yandle, A. Pandey, M. Bonaparte, K Yin, A. Pallez, N. Otmani, H. Velasco, A. Meramo, A. Shrestha, Y. Davis, I. Gregoire, S. Orlowski, D. McDonough, H. Tekfi, Al Fontvieille, L. Urcuyo, Q. Deng, R. Wang, S. Marszalek, T. Mallett-Moore, M. Lardon, B. Germain, A. Trebaul, M. Bayet, S. Samson, B. Coudsy, J. Nealon, R. Harris, C. Guzman, K. Yin, M. Loiacono, S. Pépin, I. De Bruijn, D. Greenberg, I. Bruyère

BARDA

- C. Oshansky, R. Donis, R. Gorman, K. Lu, B. Yeh, C. Pavetto, E. Mcgurrin

Moderna

- H. Bennett, J. Vanas, A. Sutherland, D. Manzo, A. Figueroa, B. Leav, M. Rossi, W. Saroian, C. Crocker, B. Kuter, J. Miller

Thank you

Questions?