Efficacy Results of FLUCELVAX Quadrivalent (ccIIV4) in Subjects ≥2 years to <18 years

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OUTLINE

- Background
- Phase III Randomized Clinical Trial
  - Objectives
  - Design
  - Location & Demographics
  - Results
    - Efficacy
    - Safety
- Conclusion

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BACKGROUND

- **Cell-based influenza vaccines avoid egg adaptation, thus potentially resulting in a closer match to selected vaccine strains by FDA/WHO[1]**

- **ccIIV4 was licensed for the prevention of influenza in subjects ≥4 years of age by the U.S. Food and Drug Administration (FDA) in 2016 based on immunogenicity and safety data**

- **This is the first efficacy study with a quadrivalent cell-based influenza vaccine in a pediatric population and is a FDA requirement to demonstrate efficacy in this population**

1. Pérez Rubio A & Eiros JM. *Hum Vaccin Immunother.* 2018;14:1874–1882

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STUDY OBJECTIVES

- **Primary:** Demonstrate vaccine efficacy (VE) of ccIIV4 in preventing influenza vs non-influenza comparator vaccine†
  - **SUCCESS**: Lower limit of the 2-sided 95% confidence interval for VE exceeds 20%

- **Secondary:** Demonstrate VE of ccIIV4 in preventing influenza due to any and vaccine-matched strains

- Immunogenicity: Characterization of immune response by HI and MN assays in a subset of subjects

- **Safety and Tolerability:** Solicited and unsolicited adverse events throughout the study

†MenACWY conjugate vaccine; Menveo®, GlaxoSmithKline Biologicals

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VACCINE TRIAL DESIGN

- **Double Blind Placebo Controlled Trial / Randomized in a 1:1 fashion**
  - **ccIIV4** 60 µg/0.5 mL pre-filled syringe, IM
    - ✓ Season 1 - **ccIIV4 Southern** Hemisphere 2017
    - ✓ Season 2 - **ccIIV4 Northern** Hemisphere 2017/2018
    - ✓ Season 3 - **ccIIV4 Northern** Hemisphere 2018/2019
  - **Non-Influenza Comparator**
    - ✓ Menveo: conjugate MenACWY (CRM_{197}) vaccine, 0.5 mL, IM
    - ✓ Second dose placebo 0.9% saline, 0.5 mL, IM
  - **Previously Vaccinated (2/3 of study population)**
    - **Any subject 9 yrs. to <18 yrs., or any subject 2 yrs. to <9 yrs. who had received 2 or more flu vaccines prior to enrollment**
  - **Previously Not Vaccinated (1/3 of study population)**
    - **Any subject 2 yrs. to <9 yrs. who had not received 2 or more doses of flu vaccine prior to enrollment**

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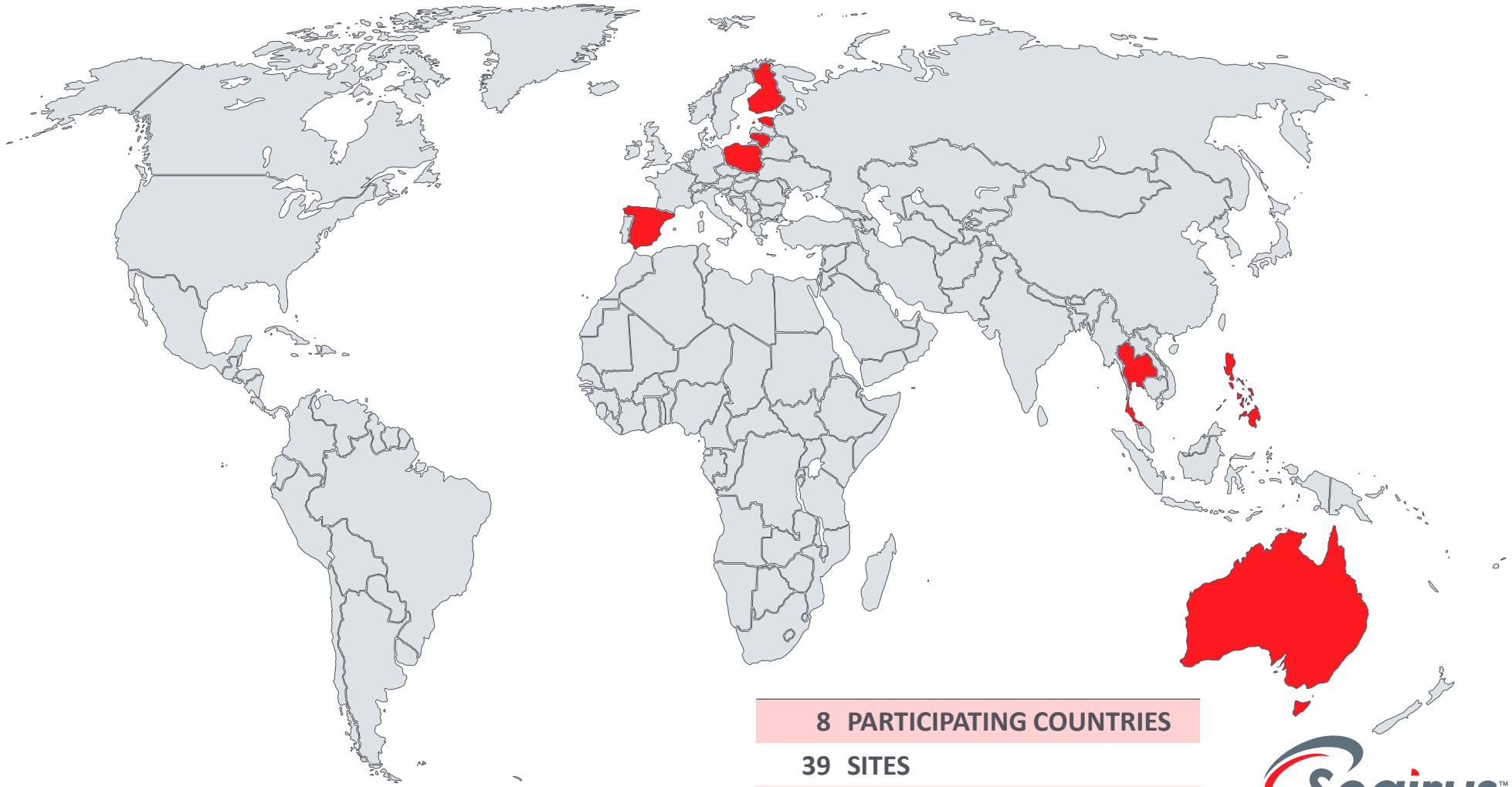
PARTICIPATING COUNTRIES

SEASON 1 S HEMISP. 2017	
PHILIPPINES	1800
THAILAND	400
AUSTRALIA	195
TOTAL	**2395**

SEASON 2 N HEMISP. 2017/18	
ESTONIA	600
FINLAND	319
TOTAL	**919**

SEASON 3 N HEMISP. 2018/19	
ESTONIA	598
POLAND	298
LITHUANIA	292
FINLAND	7
SPAIN	5
TOTAL	**1200**



8	PARTICIPATING COUNTRIES
39	SITES
4514	TOTAL ENROLLMENT

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DEMOGRAPHICS AND BASELINE CHARACTERISTICS

		ccIIV4 N=2258	Control† N=2256
Age	Mean (SD)	8.7 (4.0)	8.9 (4.1)
Sex	Male, n (%)	1152 (51.0)	1174 (52.0)
	Female, n (%)	1106 (49.0)	1082 (48.0)
Race	Asian, n (%)	1106 (49.0)	1100 (48.8)
	White, n (%)	1140 (50.5)	1139 (50.5)
	Other, n (%)	11 (0.5)	15 (0.7)
Prior vaccination status	Previously vaccinated, n (%)	1488 (65.9)	1487 (65.9)
	Not previously vaccinated, n (%)	770 (34.1)	769 (34.1)
Season	SH 2017, n (%)	1199 (53.1)	1196 (53.0)
	NH 2017-2018, n (%)	459 (20.3)	460 (20.4)
	NH 2018-2019, n (%)	600 (26.6)	600 (26.6)

†MenACWY conjugate vaccine; Menveo®, GlaxoSmithKline Biologicals

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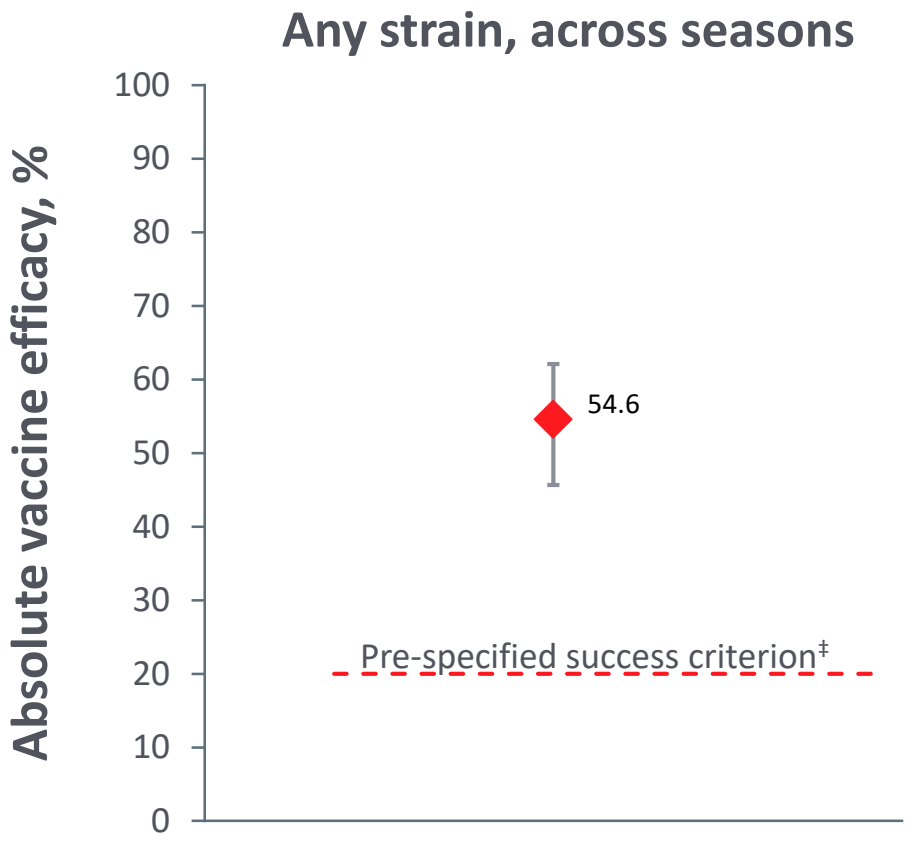
PRIMARY OBJECTIVE: ABSOLUTE VACCINE EFFICACY
RT-PCR CONFIRMED INFLUENZA



Any strain	ccIIV4 N=2257 n (attack rate)	Control† N=2252 n (attack rate)	aVE % (95% CI)
Overall RT-PCR-confirmed cases	175 (7.8)	364 (16.2)	54.6 (45.7, 62.1)

- **ccIIV4 prevented RT-PCR confirmed influenza (any Influ. A or B strain), with an absolute vaccine efficacy of 54.6%**
- **Pre-specified criterion for success was met**

The lower bound of the 95% CI exceeded 20%
†MenACWY conjugate vaccine; Menveo®, GlaxoSmithKline Biologicals

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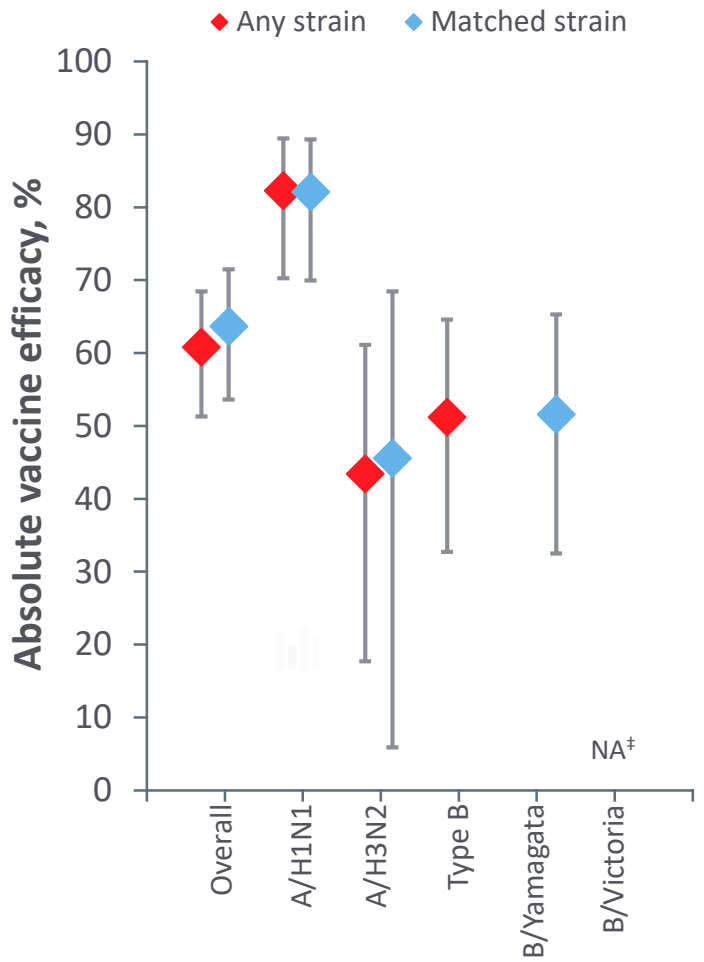
SECONDARY OBJECTIVE: ABSOLUTE VACCINE EFFICACY
CULTURE-CONFIRMED INFLUENZA BY ANY STRAIN VS MATCHED STRAIN



Strain	ccIIV4, N=2257 % (95%CI) Any	% (95% CI) Matched
Overall	**60.8** (51.3, 68.5)	**63.6** (53.6, 71.5)
A/H1N1	**82.3** (70.3, 89.4)	**82.1** (69.9, 89.3)
A/H3N2	**43.4** (17.7, 61.1)	**45.5** (5.9, 68.5)
Type B	**51.2** (32.7, 64.6)	NA
B/Yamagata	NA	**51.6** (32.5, 65.3)
B/Victoria	NA	NA‡

‡Not estimable, due to insufficient circulating strain.

aVE, absolute vaccine efficacy; CI, confidence interval; NA, not available; RT-PCR, reverse transcription polymerase chain reaction.

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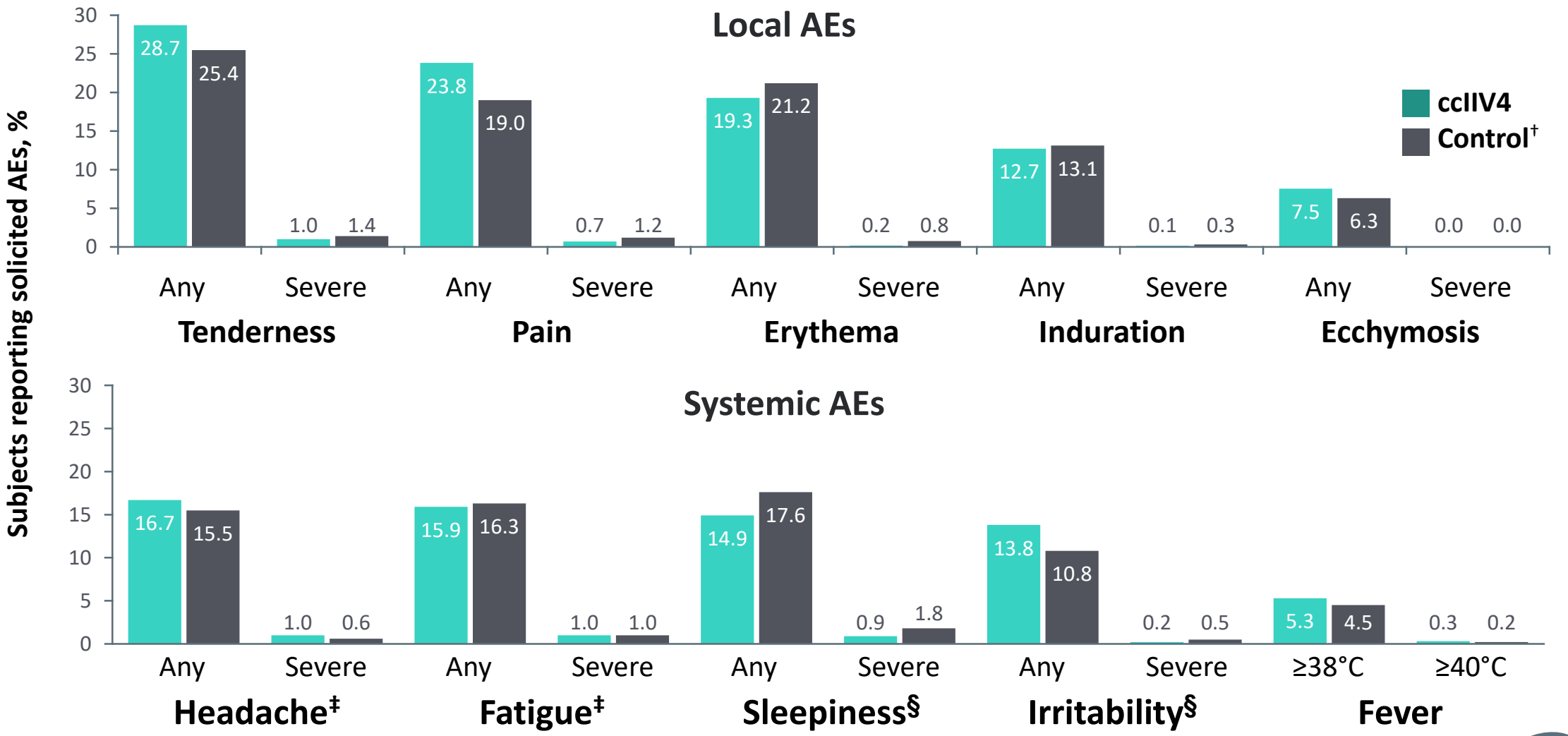
SOLICITED LOCAL AND SYSTEMIC ADVERSE EVENTS



†MenACWY conjugate vaccine; Menveo®, GlaxoSmithKline Biologicals
‡Collected on diary card for subjects age ≥6 years only; §Collected on diary card for subjects aged 2 to <6 years only.
AE, adverse event; ccIIV4, cell-based quadrivalent influenza vaccine.

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FLUCELVAX Quadrivalent (ccIIV4) CONCLUSIONS

- First efficacy study with a cell-derived quadrivalent influenza vaccine in the Pediatric and Adolescent population (2-18 years)
- Overall vaccine efficacy was 54.6% (95% CI 45.7, 62.1)†
- ccIIV4 was well tolerated, with similar rates of solicited and unsolicited adverse events between the two vaccination groups

†The lower bound of the 95% CI exceeded 20%
CI, confidence intervals

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Thank you

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ABSOLUTE VACCINE EFFICACY BY SEASON
FIRST-OCCURRENCE RT-PCR- OR CULTURE-CONFIRMED INFLUENZA

Season	Season 1			Season 2			Season 3		
	QIVc	Comparator	aVE[a] (95%CI)	QIVc	Comparator	aVE[a] (95%CI)	QIVc	Comparator	aVE[a] (95%CI)
Strain	**N=1198**	**N=1193**		**N=459**	**N=459**		**N=600**	**N=600**	
Any Strain - Number of cases (attack rate)	**89 (7.4)**	**193 (16.2)**	**56.58 (44.18; 66.22)**	**47 (10.2)**	**80 (17.4)**	**44.16 (19.93; 61.05)**	**39 (6.5)**	**91 (15.2)**	**59.49 (41.03; 72.18)**
Type A	48 (4.0)	101 (8.5)	54.15 (35.35; 67.48)	11 (2.4)	25 (5.4)	57.39 (13.40; 79.04)	37 (6.2)	88 (14.7)	60.26 (41.63; 72.94)
A/H1N1	6 (0.5)	42 (3.5)	86.16 (67.45; 94.12)	0 (0)	3 (0.7)	NA (NA; NA)	15 (2.5)	60 (10.0)	76.26 (58.17; 86.53)
A/H3N2	30 (2.5)	55 (4.6)	46.20 (16.06; 65.52)	11 (2.4)	21 (4.6)	49.03 (-5.73; 75.43)	19 (3.2)	26 (4.3)	28.28 (-29.61; 60.32)
Type B	42 (3.5)	92 (7.7)	55.95 (36.55; 69.42)	36 (7.8)	55 (12.0)	36.01 (2.57; 57.97)	3 (0.5)	3 (0.5)	NA (NA; NA)

Source: Table 14.2.0.1.3.1.

Abbreviations: aVE = absolute vaccine efficacy; CI = confidence interval; Men ACWY = meningococcal (Serogroup ACWY) conjugate vaccine; QIVc = cell-derived quadrivalent subunit influenza virus vaccine.

[a] Adjusted aVE is presented.

Note 1: The non-influenza comparator is meningococcal (Serogroup ACWY) conjugate vaccine. Previously vaccinated subjects under 9 years of age received 1 vaccination (QIVc or Men ACWY) on Day 1. For subjects under 9 years of age who had not been previously vaccinated, 2 vaccinations were administered; the comparator vaccine group received Men ACWY on Day 1 followed by a saline placebo vaccine on Day 29, whereas the QIVc group received 2 QIVc vaccinations on Days 1 and 29.

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