

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Osorio JE, Velez ID, Thomson C, et al. Safety and immunogenicity of a recombinant live attenuated tetravalent dengue vaccine (DENVax) in flavivirus-naive healthy adults in Colombia: a randomised, placebo-controlled, phase 1 study. *Lancet Infect Dis* 2014; published online July 24. [http://dx.doi.org/10.1016/S1473-3099\(14\)70811-4](http://dx.doi.org/10.1016/S1473-3099(14)70811-4).

	Low-dose subcutaneous		Low-dose intradermal		High-dose subcutaneous		High-dose intradermal		Overall	
	DENVax (n=19)	Placebo (n=5)	DENVax (n=21)	Placebo (n=3)	DENVax (n=21)	Placebo (n=4)	DENVax (n=18)	Placebo (n=5)	DENVax (n=79)	Placebo (n=17)
After first dose										
Solicited systemic adverse events	16 (84%)	4 (80%)	16 (76%)	1 (33%)	16 (76%)	2 (50%)	16 (89%)	4 (80%)	64 (81%)	11 (65%)
Fever	1 (5%)	1 (20%)	2 (10%)	0	1 (5%)	0	1 (6%)	0	5 (6%)	1 (6%)
Headache	11 (60%)	2 (40%)	11 (52%)	1 (33%)	9 (43%)	1 (25%)	8 (44%)	2 (40%)	39 (49%)	6 (35%)
Muscle pain	8 (42%)	0	2 (10%)	1 (33%)	5 (24%)	0	6 (33%)	0	21 (27%)	1 (6%)
Joint pain	5 (26%)	0	1 (5%)	0	2 (10%)	0	3 (17%)	0	11 (14%)	0
Eye pain	7 (37%)	1 (20%)	8 (38%)	0	3 (14%)	1 (25%)	2 (11%)	2 (40%)	20 (25%)	4 (24%)
Photophobia	3 (16%)	0	2 (10%)	0	2 (10%)	1 (25%)	3 (17%)	2 (40%)	10 (13%)	3 (18%)
Fatigue	10 (53%)	1 (20%)	6 (29%)	0	5 (24%)	0	10 (56%)	4 (80%)	31 (39%)	5 (29%)
Body rash	0	0	1 (5%)	0	2 (10%)	0	4 (22%)	0	7 (9%)	0
Nausea	5 (26%)	2 (40%)	5 (24%)	0	5 (24%)	0	4 (22%)	2 (40%)	19 (24%)	4 (24%)
Vomiting	0	0	0	0	1 (5%)	0	1 (6%)	0	2 (3%)	0
Other	6 (37%)	1 (20%)	5 (24%)	0	11 (52%)	2 (50%)	5 (28%)	2 (40%)	27 (34%)	5 (29%)
After second dose										
Solicited systemic adverse events	10 (53%)	2 (40%)	15 (71%)	1 (33%)	10 (48%)	1 (25%)	13 (72%)	2 (40%)	48 (61%)	6 (35%)
Fever	2 (11%)	0	1 (5%)	1 (33%)	0	1 (25%)	1 (6%)	0	4 (5%)	2 (12%)
Headache	5 (27%)	1 (20%)	11 (52%)	1 (33%)	5 (24%)	0	9 (50%)	1 (20%)	30 (38%)	3 (18%)
Muscle pain	3 (16%)	0	3 (14%)	1 (33%)	2 (10%)	0	2 (11%)	0	10 (13%)	1 (6%)
Joint pain	1 (5%)	0	2 (10%)	0	2 (10%)	0	0	0	5 (6%)	0
Eye pain	3 (16%)	1 (20%)	5 (24%)	1 (33%)	1 (5%)	0	7 (39%)	1 (20%)	16 (20%)	3 (17%)
Photophobia	2 (11%)	1 (20%)	5 (24%)	1 (33%)	3 (14%)	0	2 (11%)	0	12 (15%)	2 (12%)
Fatigue	7 (37%)	1 (20%)	7 (33%)	1 (33%)	4 (19%)	0	10 (56%)	1 (20%)	28 (35%)	3 (18%)
Body rash	0	0	0	1 (33%)	0	0	0	0	0	1 (6%)
Nausea	2 (11)	0	2 (10)	1 (33)	1 (5)	0	5 (28)	0	10 (13)	1 (6)
Vomiting	1 (5)	0	0	0	1 (5)	0	2 (11)	0	4 (5)	0
Other	3 (16)	0	3 (14)	0	5 (24)	0	1 (6)	1 (20)	12 (15)	1 (6)

Data are n (%), unless otherwise indicated.

Table 1: Number of patients with solicited systemic adverse events after the first or the second dose

	Low-dose subcutaneous		Low-dose intradermal		High-dose subcutaneous		High-dose intradermal		Overall	
	DENVax (n=19)	Placebo (n=5)	DENVax (n=21)	Placebo (n=3)	DENVax (n=21)	DENVax (n=19)	Placebo (n=5)	DENVax (n=21)	Placebo (n=3)	DENVax (n=21)
After first dose										
Solicited local adverse events	13 (68%)	1 (20%)	17 (81%)	1 (33%)	14 (66%)	1 (25%)	18 (100%)	1 (20%)	62 (79%)	4 (24%)
Pain	12 (63%)	1 (20%)	6 (27%)	1 (33%)	4 (19%)	0	11 (61%)	1 (20%)	33 (42%)	3 (18%)
Redness	6 (32%)	0	17 (81%)	0	11 (52%)	1 (25%)	16 (89%)	0	50 (63%)	1 (6%)
Swelling	5 (26%)	0	6 (29%)	0	6 (29%)	0	6 (33%)	0	23 (29%)	0
Itching	3 (16%)	0	5 (24%)	0	7 (33%)	1 (25%)	8 (44%)	1 (20%)	23 (29%)	2 (12%)
After second dose										
Solicited local adverse events	11 (58%)	0	19 (91%)	2 (66%)	8 (38%)	0	15 (83%)	0	53 (67%)	2 (12%)
Pain	8 (42%)	0	4 (19%)	2 (66%)	7 (33%)	0	5 (28%)	0	24 (30%)	2 (12%)
Redness	2 (11%)	0	19 (91%)	0	6 (29%)	0	12 (67%)	0	39 (49%)	0
Swelling	1 (5%)	0	12 (57%)	0	3 (14%)	0	6 (33%)	0	22 (28%)	0
Itching	4 (21%)	0	10 (48%)	1 (33%)	2 (10%)	0	12 (67%)	0	28 (35%)	1 (6%)

Data are n (%), unless otherwise indicated. Percentages are based on the number of patients in the safety population (including the five who withdrew who did not receive a second dose).

Table 2: Number of patients with solicited local adverse events after the first or the second dose

	Day 0	Day 7	Day 14	Day 21	Day 90	Day 97	Day 104
Haemoglobin (g/L)							
DENVax	150 (17)	147 (15)	145 (16)	146 (16)	148 (17)	145 (17)	146 (17)
Placebo	146 (15)	146 (19)	144 (18)	146 (17)	148 (19)	146 (20)	144 (19)
White-blood-cell count (10⁹/L)							
DENVax	7.3 (1.7)	6.5 (1.4)	7.0 (1.7)	7.3 (1.6)	7.1 (1.4)	7.2 (2)	7.3 (1.8)
Placebo	7.1 (1.1)	6.8 (1.1)	7.2 (1.6)	6.5 (1)	6.7 (1)	7.2 (1)	7.0 (1.3)
Neutrophils (10⁹/L)							
DENVax	4.3 (1.6)	3.6 (1.3)	4.2 (1.5)	4.0 (1.4)	4.0 (1.2)	4.2 (1.9)	4.2 (1.4)
Placebo	3.9 (1)	3.8 (1)	4 (1)	3.5 (0.8)	3.7 (1.0)	4.0 (0.8)	3.9 (0.9)
Platelet Counts (10⁹/L)							
DENVax	254 (69)	244 (60)	249 (60)	261 (63)	248 (60)	254 (61)	260 (64)
Placebo	260 (66)	247 (46)	246 (47)	239 (35)	232 (35)	246 (38)	253 (41)
Prothrombin time (s)							
DENVax	14.8 (1)	14.7 (1)	14.5 (1)	14.6 (1)	15.2 (1)	15.2 (1)	14.8 (1)
Placebo	14.6 (0.7)	14.6 (0.7)	14.4 (1)	14.1 (0.6)	14.9 (0.8)	14.9 (0.9)	14.9 (1.2)
Partial thromboplastin time (s)							
DENVax	32.9 (3)	32.1 (3)	31.6 (3)	33.3 (3.5)	34.4 (3.5)	32.9 (3.5)	32.3 (2.9)
Placebo	33.1 (3.5)	33.4 (4)	31.6 (4.1)	33.6 (3)	34.1 (3.8)	32.7 (3.3)	32.6 (3.3)
Fibrinogen (g/L)							
DENVax	2.8 (0.6)	3.1 (0.6)	3.1 (0.6)	2.9 (0.6)	2.9 (0.5)	3.0 (0.7)	3.0 (0.6)
Placebo	3.0 (0.4)	3.1 (0.6)	2.9 (0.5)	2.9 (0.5)	3.0 (0.5)	3.1 (0.7)	3.0 (0.5)
ALT (IU/L)							
DENVax	21.3 (18)	21.9 (16)	21.9 (17)	22.4 (14)	20.9 (14)	20.5 (11)	18.7 (10.2)
Placebo	19.2 (9)	18.4 (8.5)	16.4 (6)	17.6 (7.5)	20.8 (16.6)	17.9 (11.5)	21.9 (6.2)
AST (IU/L)							
DENVax	25.4 (31)	23.0 (11.4)	22.4 (8.8)	22.4 (7.7)	22.4 (7.7)	21.3 (5.9)	21.9 (6.2)
Placebo	22.2 (5.3)	22.0 (8.1)	19.2 (4.2)	21.5 (6)	23 (13)	19.8 (5.1)	21.5 (5.1)

Data are mean (SD). ALT=alanine transaminase. AST=aspartate transaminase.

Table 3: Clinical laboratory findings after DENVax administration