GENERAL INFORMATION OF THE CLINICAL TRIAL

RPCEC code	RPCEC00000374
Public title	SOBERANA PEDIATRIA
Scientific title	Phase I-II study, sequential during phase I, open-label, adaptive and multicenter to evaluate the safety, reactogenicity and immunogenicity, of a heterologous two-dose schedule of the prophylactic anti-SARS vaccine candidate - CoV-2, FINLAY-FR- 2 and a dose of FINLAY-FR-1A, in Cuban children and adolescents. (COVID-19)
Intervention description	Experimental Group: FINLAY-FR-2 + FINLAY-FR-1A. FINLAY-FR-2: 25 µg of RBD-TT, by intramuscular route, 0.5 mL, in scheme 0 - 28 days. FINLAY-FR-1A: 50 µg of d-RBD + Aluminum Hydroxide Gel, by intramuscular route, 0.5 mL as dose booster 56 days.

PARTICIPANT FLOW

Assessed for eligibility	436
Excluded	86
Excluded - Causes	
History of chronic diseases	9
Weight-height nutritional assessment below the 10th and 90th percentile (for subjects between 3 and 9 years of age) or the Body Mass Index below the 10th and above the 90th percentile for subjects between 10 and 18 years of age), according to the cut-off points for the Cuban pediatric population	44
Subjects that meet any of the following criteria: a) Previous or current history of SARS-CoV 2 infection. B) SARS-CoV 2 PCR positive. C) Be declared in the category of contact or suspect at the time of inclusion	7
Laboratory results outside the range of reference values that are clinically significant (For the subjects to be included in phase I)	3
Not giving informed consent for participation in the study (one of the parents is missing)	4
History of allergy with treatment	4
Subjects with a history of Convulsive Disease	1
General, regional and apparatus physical examination with alterations	2
Subjects with a history of having received a vaccine from the Cuban immunization scheme, in a period of less than 30 days prior to the administration of the product under investigation	3
Subjects with acute febrile or infectious disease at the time of the vaccine application or in the 7 days prior to its administration	2
History of severe allergic reactions	7
Enrolled	350
Not completed the study	44
Not completed the study - Causes	

PCR+ to SARS-CoV-2	42
Voluntary abandonment	2
Completed the study	306
Used in analysis after two doses	318
Used in analysis after three doses	306

BASELINE CHARACTERISTICS

The results are shown according to the age groups analyzed: 3-11 years and 12-18 years.

	Age groups		
	3 -11 years	**12 -18 years**	**Total**
N	175	175	350
Sex			
Female	80 (45.7%)	83 (47.4%)	163 (46.6%)
Male	95 (54.3%)	92 (52.6%)	187 (53.4%)
Skin color			
White	122 (69.7%)	116 (66.3%)	238 (68.0%)
Black	9 (5.1%)	11 (6.3%)	20 (5.7%)
Mixed	44 (25.1%)	48 (27.4%)	92 (26.3%)
Age (years)			
Mean (SD)	7.4 (2.5)	15.1 (2.1)	11.3 ± 4.5
Median (IQR)	8.0 (5.0)	15.0 (4.0)	11.5 ± 7.0
Rank	3; 11	12;18	3-18
Weight (kg)			
Mean (SD)	29.4 (10.1)	54.7 (9.0)	42.0 ± 15.9
Median (IQR)	27.5 (14.0)	55.0 (13.0)	43.0 ± 27.7
Rank	13.0; 58.0	32.0; 80.0	13.0; 80.0
Size (cm)			
Mean (SD)	129.1 (17.2)	164.3 (9.6)	146.7 ± 22.5
Median (IQR)	131.0 (26.0)	164.0 (13.0)	151.0 ± 34.0
Rank	92; 172	142; 190	92-190
BMI (kg/m^2)			
Mean (SD)	17.0 (2.0)	20.2 (2.3)	18.6 ± 2.7
Median (IQR)	16.7 (2.7)	19.9 (3.8)	18.3 ± 4.1
Rank	13.2; 22.8	14.6; 25.5	13.2-25.5

Data given in n (%) unless otherwise specified.
SD= Standard Deviation, IQR= Interquartile Range, BMI=Body Mass Index, Range=(Minimum; Maximum)

OUTCOME MEASURES

The results consider the 350 subjects enrolled in Phase I-II with ages between 12-18 and 3-11 years.

a) Primary outcomes

Phase I: Serious Adverse Events-SAE (It will measure as: -Occurrence of the SAE (Yes, No), -Duration (Time from start date until end date of event), -Description of the event, Result (Recovered, Recovered with squeals, Persists, Death, Unknown), - Causality (Causal association consistent with vaccination, Undetermined, Inconsistent causal association with vaccination, not classifiable). Measurement time: daily for 28 days after each dose

	Age group		
	3-11 years	**12-18 years**	**Total**
N	175	175	350
Subjects with any serious AE	0 (0.0%)	1* (0.6%)	1 (0.3%)
Subjects with any serious AE related	0 (0.0%)	0 (0.0%)	0 (0.0%)
AE serious related	0 (0.0%)	0 (0.0%)	0 (0.0%)
AE severe related	0 (0.0%)	0 (0.0%)	0 (0.0%)
AE= Adverse event. * SAE: Dengue required hospitalization.			

This variable was a secondary outcome in a Phase II.

Phase II: Concentration of specific anti-RBD IgG antibodies (Percentage of subjects with seroconversion 4-fold to pre-vaccination). Measurement time: Day 0, 42 and 70

		Age group						PNC
		3-11 years		12-18 years		Total		
		Post-2nd dose	Post-3rd dose	Post-2nd dose	Post-3rd dose	Post-2nd dose	Post-3rd dose	
N		159	156	159	150	318	306	82
IgG Anti-RBD seroconversion	N (%)	157/158 (99.4)	155/155 (100.0)	148/159 (93.1)	150/150 (100%)*	305/317 (96.2)	305/305 (100.0)*	N.D
	IC 95%	96.5; 99.9	99.6; 100.0	88.0; 96.5	99.6; 100.0	93.5; 98.0	99.8; 100.0	
T0 IgG anti-RBD 1.95 (25-75 percentile 1.95; 1.95) for both subgroups and total. ND: Undetermined Seroconversion index: increase in IgG concentrations compared to T0 IC 95%= confidence interval at 95%; 25-75= percentiles 25-75. * p<0.005 versus Post – 2nd dose test of McNemar (% of seroconversion IgG anti-RBD), test of Wilcoxon (IgG anti-RBD, % Inh RBD:hACE2) or test t de Student ($mVNT_{50}$, $cVNT_{50}$, log-transformed). PNC= Panel of convalescent children.								

This variable was a secondary outcome in a Phase I.

b) Secondary outcomes

1) Adverse Events (AE) solicited local and systemic (They will be measured as: - Occurrence of AE (Yes, No), Duration (Time from start to the end of AE), - Intensity of AE (mild, moderate, severe), - Severity (Serious, not serious), - Result (Recovered, Recovered with aftermath, Persists, Death, Unknown), - Causality (Causal association consistent with vaccination, Undetermined, Causal association inconsistent with vaccination, Unclassifiable). Measurement time: daily for 3 days after each dose

	Age group		
	3-11 years	**12-18 years**	**Total**
N	175	175	350
Subjects with some AE	81 (46.3%)	105 (60.0%)	186 (53.10%)
Subjects with some solicited local AE			
Some AE	74 (42.3%)	98 (56.0%)	172 (49.1%)
Local pain	69 (39.4%)	98 (56.0%)	167 (47.7%)
Volume increase	9 (5.1%)	2 (1.1%)	11 (3.1%)
Local heat	4 (2.3%)	0 (0.0%)	4 (1.1%)
Erythema	5 (2.9%)	1 (0.6%)	6 (1.7%)
Induration	5 (2.9%)	1 (0.6%)	6 (1.7%)
Subjects with some solicited systemic AE			
Some AE	5 (2.9)	4 (2.3)	9 (2.6)
General discomfort	1 (0.6%)	3 (1.7%)	4 (1.1%)
Fever (≥38 ◦C)	2 (1.1)	1 (0.6)	3 (0.9)
Low-grade fever (<38 ◦C)	4 (2.3)	1 (0.6)	5 (1.4)
AE= Adverse Event			

Frequency of subjects with adverse events per dose

		Age group		
		3-11 years	**12-18 years**	**Total**
N		175	175	350
Adverse events during the 28 days after vaccination				
Subjects with some AE		81 (46.3)	105 (60.0)	186 (53.1)
	Dose 1	54/175 (30.9)	98/175 (56.0)	152/350 (43.4)
	Dose 2	29/162 (17.9)	29/159 (18.2)	58/321 (18.1)
	Dose 3	30/156 (19.2)	31/150 (20.7)	61/306 (19.9)
Subjects with solicited AE within 7 days after vaccination				
Some AE		76 (43.4)	98 (56.0)	174 (49.7)
	Dose 1	50/175 (28.6)	90/175 (51.4)	140/350 (40)
	Dose 2	27/162 (16.7)	27/159 (17.0)	54/321 (16.8)

	Age group		
	3-11 years	**12-18 years**	**Total**
Dose 3	29/156 (18.6)	28/150 (18.7)	57/306 (18.6)
Subjects with some solicited local EA			
Some AE	74 (42.3)	98 (56.0)	172 (49.1)
Dose 1	50/175 (28.6)	90/175 (51.4)	140/350 (40)
Dose 2	27/162 (16.7)	27/159 (17.0)	54/321 (16.8)
Dose 3	26/156 (16.7)	27/150 (18.0)	53/306 (17.3)
Local pain	69 (39.4)	98 (56.0)	167 (47.7)
Dose 1	49/175 (28)	90/175 (51.4)	139/350 (39.7)
Dose 2	23/162 (14.2)	27/159 (17.0)	50/321 (15.6)
Dose 3	19/156 (12.2)	26/150 (17.3)	45/306 (14.7)
Volume increase	9 (5.1)	2 (1.1)	11 (3.1)
Dose 1	2/175 (1.1)	0/175 (0.0)	2/350 (0.6)
Dose 2	3/162 (1.9)	0/159 (0.0)	3/321 (0.9)
Dose 3	6/156 (3.8)	2/150 (1.3)	8/306 (2.6)
Local heat	4 (2.3)	0 (0.0)	4 (1.1)
Dose 1	0/175 (0.0)	0/175 (0.0)	0/350 (0.0)
Dose 2	2/162 (1.2)	0/159 (0.0)	2/321 (0.6)
Dose 3	2/156 (1.3)	0/150 (0.0)	2/306 (0.7)
Erythema	5 (2.3)	1 (0.6)	6 (1.7)
Dose 1	0/175 (0.0)	0/175 (0.0)	0/350 (0.0)
Dose 2	2/162 (1.2)	0/159 (0.0)	2/321 (0.6)
Dose 3	4/156 (2.6)	1/150 (0.7)	5/306 (1.6)
Induration	5 (2.3)	1 (0.6)	6 (1.7)
Dose 1	2/175 (1.1)	0/175 (0.0)	2/350 (0.6)
Dose 2	1/162 (0.6)	0/159 (0.0)	1/321 (0.3)
Dose 3	3/156 (1.9)	1/150 (0.7)	4/306 (1.3)
Subjects with some solicited systemic AE			
Some AE	5 (2.9)	4 (2.3)	9 (2.6)
Dose 1	1/175 (0.6)	3/175 (1.7)	4/350 (1.1)
Dose 2	0/162 (0.0)	0/159 (0.0)	0/321 (0.0)
Dose 3	4/156 (2.6)	1/150 (0.7)	5/306 (1.6)
Low-grade fever (<38 °C)	4 (2.3)	1 (0.6)	5 (1.4)
Dose 1	0/175 (0.0)	1/175 (0.6)	1/350 (0.3)
Dose 2	0/162 (0.0)	0/159 (0.0)	0/321 (0.0)
Dose 3	4/156 (2.6)	0/150 (0.0)	4/306 (1.3)
Fever (≥38 °C)	2 (1.1)	1 (0.6)	3 (0.9)
Dose 1	1/175 (0.6)	0/175 (0.0)	1/350 (0.3)
Dose 2	0/162 (0.0)	0/159 (0.6)	0/321 (0.3)
Dose 3	1/156 (0.1)	1/150 (0.7)	2/306 (0.7)
General discomfort	1 (0.6)	3 (1.7)	4 (1.1)
Dose 1	0/175 (0.0)	3/175 (1.7)	3/350 (0.9)
Dose 2	0/162 (0.0)	0/159 (0.0)	0/321 (0.0)
Dose 3	1/156 (0.6)	0/150 (0.0)	1/306 (0.3)

2) Unsolicited Adverse Events (AEs) (Will be measured as: Description of the AE (name of the event), -Duration (Time from the beginning to the end of the AE), -Intensity of the AE (mild, moderate, severe), -Severity (Severe, not serious), -Result (Recovered, Recovered with sequelae, Persists, Death, Unknown), -Causality (Causal association consistent with vaccination, Undetermined, Causal association inconsistent with vaccination, unclassifiable)). Measurement time: daily for 28 days after each dose.

	Age group		
	3-11 years	**12-18 years**	**Total**
N (%)	175	175	350
Number of subjects with unsolicited AE	14 (8.0)	21 (12.0)	35 (10.0)
Consistent with vaccination	5 (2.9)*	10 (5.7)**	15(4.3)
Headache	2 (1.1)	9 (5.1)	11 (3.1)
Not consistent	9 (5.1)***	13 (7.4)****	22 (6.3)
Headache	1 (0.6)	2 (1.1)	3 (0.9)
*Reported by 1 subject (0.6%, each): arm cramp, drowsiness, feeling of weight in the arm. ** Reported by 1 subject (0.6%, each): arm cramp *** Reported by 1 subject (0.6%, each): diarrhea; gastrointestinal disease; epistaxis; furuncle in the ear; foot wound; viral process; Nasal secretion; cough **** Reported by 1 subject (0.6%, each): thigh cellulite, tonsillitis; miliaria; dengue; diarrhea; fever; low-grade fever, hypertension; acute respiratory infection; abdominal discomfort; Nasal secretion; cough. Reported by 2 subjects (1.1% each): vomiting; nausea, diarrhea			

3) Neutralizing antibody titer: Measurement time: Day 42 and 70.

4) % ACE2-RBD inhibition: Measurement time: Day 0, 42 and 70.

		Age group				**Total**		**PNC**
		3-11 years		**12-18 years**				
		Post-2nd dose	Post-3rd dose	Post-2nd dose	Post-3rd dose	Post-2nd dose	Post-3rd dose	
	N	159	156	159	150	318	306	82
IgG Anti-RBD UA/mL	Median	93.3	329.8*	49.9	325.6*	57.0	325.7*	11.5
	25-75	39.0; 214.4	162.9; 685.6	22.3; 90.7	108.0; 555.8	29.8; 153.4	141.5; 613.8	5.3; 24.2
Seroconversion index	Median	42.6	155.4*	24.8	154.3*	27.8	154.5*	N.D
	25-75	19.5; 97.0	75.4; 260.2	11.0; 44.7	50.2; 266.3	14.3; 69.0	67.2; 260.9	
% Inh RBD:hACE2	Median	78.3	92.5*	60.1	92.2*	67.4	92.4*	20.8
	25-75	49.4; 88.9	88.8; 93.4	36.7; 79.7	87.7; 93.6	42.1; 86.9	88.3; 93.5	10.9; 40.8
$mVNT_{50}$	MGT	274.1	1418.3*	143.7	1116.2*	198.5	1261.2*	35.2
	IC 95%	216.8; 346.5	1180.0; 1704.7	115.0; 179.5	924.0; 1348.3	168.4; 233.9	1105.5; 1438.8	25.3; 48.9
$cVNT_{50}$ vs D614G	N	63	66	60	65	123	131	70
	MGT	28.4	181.6*	24.4	137.9*	26.4	158.4*	9.2

		Age group				Total		PNC
		3-11 years		12-18 years				
		Post-2nd dose	Post-3rd dose	Post-2nd dose	Post-3rd dose	Post-2nd dose	Post-3rd dose	
	N	159	156	159	150	318	306	82
	IC 95%	18.5; 43.6	120.6; 273.3	17.6; 40.0	101.8; 186.9	20.2; 34.5	123.0; 204.0	6.8; 12.5

T0 IgG anti-RBD 1.95 (25-75 percentile 1.95; 1.95) for both subgroups and total. ND: Not determined
Seroconversion index: increase in IgG concentrations compared to T0.
UA/mL= arbitrary units /mL.
% Inh RBD:hACE2: % RBD interaction inhibition:hACE2 to the dilution 1/100.
$mVNT_{50}$: molecular neutralization titer; dilution that inhibits 50% of the interaction RBD:hACE2.
$cVNT_{50}$: viral neutralization titer.
MGT= Geometric mean of titles. IC 95%= confidence interval at 95%; 25-75= percentiles 25-75.
* $p<0.005$ versus Post – 2nd dose test of McNemar (% anti-RBD IgG seroconversion), test of Wilcoxon (IgG anti-RBD, % Inh RBD:hACE2) or test t de Student ($mVNT_{50}$, $cVNT_{50}$, log-transformed). PNC= Panel of convalescent children.

ADVERSE EVENTS

	Age group		Total
	3-11 years	**12-18 years**	
N	175	175	350
Subjects with some AE	81 (46.3%)	105 (60.0%)	186 (53.1%)
Subjects with some related AE	76 (43.4%)	101 (57.7%)	177 (50.6%)
Subjects with some severe AE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subjects with any related severe AE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total of AE	141	182	323
Mild	135 (95.7%)	167 (91.8%)	302 (93.5%)
Moderate	6 (4.3%)	15 (8.2%)	21 (6.5%)
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)
Locals	118 (83.7%)	147 (80.8%)	265 (82.0%)
Systemics	23 (16.3%)	35 (19.2%)	58 (18.0%)
AE consistent with vaccination	126 (89.4%)	160 (87.9)	286 (88.5%)
AE= Adverse Event			

Global characterization of adverse events

	Age group		
	3-11 years	**12-18 years**	**Total**
Total adverse events	141	182	323
Intensity			
Mild	135 (95.7)	167 (91.8)	302 (93.5)
Moderate	6 (4.3)	15 (8.2)	21 (6.5)
Severe	0	0	0
Severity			
Not serious	141 (100.0)	181 (99.5)	322 (99.7)
serious	0	1 (0.5) *	1 (0.3) *
Causality			
Consistent (A1)	126 (89.4)	160 (87.9)	286 (88.5)
Consistent (A2)	0	0	0
Consistent (A3)	0	0	0
Undetermined(B1)	0	2 (1.1)	2 (0.6)
Undetermined(B2)	0	1 (0.5)	1 (0.3)
Inconsistent	15 (10.6)	19 (10.4)	34 (10.5)
Result			
Recovered	141 (100.0)	181 (99.5)	322 (99.7)
Recovered with sequel	0	1 (0.5)*	1 (0.3)*
Type			
Local	118 (83.7)	147 (80.8)	265 (82.0)
Systemic	23 (16.3)	35 (19.2)	58 (18.0)
Requested			
Solicited (Requested)	125 (88.7)	152 (83.5)	277 (85.8)
Unsolicited (Not requested)	16 (11.3)	30 (16.5)	46 (14.2)
Begin to			
≤ 60 min	25 (13.7)	25 (17.7)	50 (15.5)
60 min-24 hours	127 (69.8)	85 (60.3)	212 (65.6)
24-48 hours	15 (8.2)	14 (9.9)	29 (9.0)
48-72 hours	1 (0.5)	3 (2.1)	4 (1.2)
> 72 hours	14 (7.7)	14 (9.9)	28 (8.7)
Duration (hours)			
≤ 24 hours	99 (54.4)	74 (52.5)	173 (53.6)
24-48 hours	37 (20.3)	35 (24.8)	72 (22.3)
48-72 hours	33 (18.1)	16 (11.3)	49 (15.2)
> 72 hours	13 (7.1)	16 (11.3)	29 (9.0)
* Dengue			